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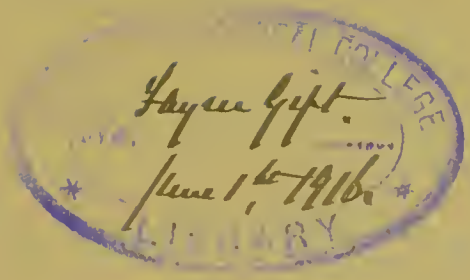

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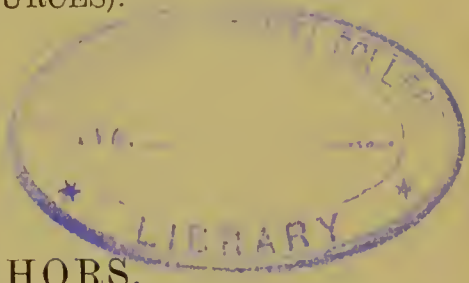

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A CONTRIBUTION

TO THE

ÆTIOLOGY OF TERTIARY SYPHILIS,

WITH SPECIAL REFERENCE TO THE

INFLUENCE OF MERCURIAL TREATMENT UPON THE DEVELOPMENT OF TERTIARY SYMPTOMS.

BY

Dr. THOMAS v. MARSCHALKO.

TRANSLATED

BY

ARCHIBALD GARROD, M.D.

ÆTIOLOGY OF TERTIARY SYPHILIS.

By Thomas v. Marschalko.

The present investigation was undertaken, at the suggestion of Professor Neisser, during the three winter sessions throughout which I was working in the dermatological clinic at Breslau. Professor Neisser urged me to enter upon a statistical investigation of the abundant material illustrative of tertiary syphilis brought together in the Breslau dermatological clinic and policlinic. This invitation I accepted the more readily because I had myself, in the course of my practice at Bad Lipik, had many opportunities, during the nine preceding years, of seeing numerous cases of tertiary syphilis, and had already at my disposal statistics of more than 100 cases. Moreover, Professor Neisser placed in my hands his own private material, and thus the opportunity was afforded of making a thorough study of a large mass of statistics drawn from several hundreds of syphilitic cases, and of instituting a comparison, which promised to prove of great interest, between the hospital and private statistics.

We felt sure, from the outset, that the questions of the causation of tertiary syphilis and of its relation to antecedent treatment could not be answered with mathematical certainty by means of retrospective statistics, and the reasons for the impossibility of doing so will be fully discussed. Nevertheless I think that our figures will show that even such statistics, when submitted to unbiased consideration, may serve to support our views on the question of treatment, and may encourage us to continue our endeavours on Fournier's lines.

I would here express my most hearty thanks to Professor Neisser for his many suggestions, for his kind permission to make use of his material, and for the interest with which he has followed my work.

Although of recent years many authors in various countries have entered upon the discussion of the pathogenesis of tertiary syphilis, they have done so less in the belief that it is possible

in this way to arrive at a knowledge of the nature of the tertiary lesions, than with the desire to arrive at the solution of the purely practical question of how syphilis is best treated.

In these discussions the chief question raised is whether we are to look upon mercury as a mere symptomatic remedy, which simply influences the symptoms of the malady, or as a remedy which exerts an influence upon the syphilitic virus itself, the judicious employment of which is not merely capable of causing the symptoms to disappear, but further of affecting the disease itself and the cause of the malady as a whole.

In spite of the abundant material which is available for the solution of this problem, we are still far from a definite answer, and indeed it is very probable that its solution is rendered more difficult by the very fact that we see the disease at all ages and under the most various conditions of life; as influenced by all sorts of external conditions, and by the various idiosyncrasies of the patients. This drives us to the conclusion that cases of syphilis are extremely protean in the courses they run, and we are unable to make sure what particular influences have shaped the course of the disease in individual cases.

Thus we speak of an "individual course," by which is indicated that we are unacquainted with the true grounds for the behaviour of special cases.

What has always appeared to be the most remarkable feature of these differences in the course of syphilis is the peculiar circumstance that whereas in most cases symptoms manifest themselves only during the first years after infection, in others, which constitute a much smaller proportion, the so-called late or tertiary symptoms are met with, manifestations which also exhibit, for decades together, the widest differences in their seat, distribution, and so on.

Indeed the difficulty often begins to be encountered in answering the simple diagnostic question, is the observed syphilitic manifestion to be regarded as tertiary?

What is the meaning of tertiary?

Although we are in a position to define roughly what we mean by tertiary syphilis, we are nevertheless, but only to some extent, without any certain basis for such a diagnosis in atypical cases. Histological investigations have not yet provided a sharp distinction between the papular and gummatous lesions, and as regards

clinical features, the numerous attempts at a systematic classification of syphilides demonstrate the difficulty of differentiating sharply between the two great groups of syphilitic growths, viz., those of the earlier and later periods. The longer we study the subject the more we come to recognise the existence of transitional forms, themselves of the most various kinds, between the secondary and tertiary lesions. Then we have also the simultaneous development of early and late symptoms, the occurrence of gummatous lesions in the earliest period of the disease, and conversely the development of papular efflorescences in the late period, an occurrence testified to on various sides. Lastly, we are completely ignorant to what extent and for how long a time there is a direct association of infectiousness with tertiary manifestations. All these causes contribute to render it impossible, with our present knowledge, to give a clear definition of the nature of tertiary syphilis.

Nevertheless the attempt is always being made—and rightly too—to gain an insight, if not into the nature of tertiary syphilis at least into some points in its ætiology, by the establishment of certain main general propositions.

It is well known that the older investigators of the disease sought the origin of tertiary syphilis in mercurial treatment itself, or at least in what they regarded as an excessive or injudicious employment of mercury.

In this connection the views of authors followed two different paths. Some held that mercury was the immediate and direct cause of the tertiary manifestations, which were regarded as nothing else than those of mercurial poisoning. This view is generally abandoned at the present day.

The other view is that the tertiary syphilis is only indirectly due to the mercury, the disease being capable of assuming a malignant course in the organism which has been altered and weakened by that drug. Thus W. Boeck[1] held that tertiary syphilis, and especially its visceral forms, were often due to mercury, the use of which caused debility, so that the organism was not in a condition to eliminate the syphilitic virus.

Again, v. Baerensprung[2] says: "Mercury does not completely cure syphilis, but the mercurialism which develops merely causes the disappearance of its visible manifestations. As long as the action of mercury is maintained the syphilis remains

latent, and afterwards reappears under a form which is the more unfavourable the more the constitution of the patient has suffered in the meantime." He further[3] says: "The further development of the morbid process is not hindered by mercury, the appearance of fresh symptoms being merely postponed with the result that the disease is prolonged; under such circumstances syphilis often passes on to its tertiary form and may ultimately become incurable." Again, in another work[4]: "Tertiary syphilis is not mercurialism, but is still syphilis, but modified syphilis; syphilis in an organism altered by mercury."

Other authors, such as Syme[5] and Hughes Bennett[6] look for the true cause of tertiary syphilis in excessive administration of mercury to patients already weakened by syphilitic dyscrasia. Gros[7] and Lancereaux[8] connect tertiary syphilitic affections of the central nervous symptoms with excessive mercurial treatment. Even that is in our opinion incorrect. In order to prove it a fact that tertiary syphilis is indirectly caused by the mercury, it would have to be shown that mercury exerts a deleterious influence upon syphilis; for instance, that syphilis assumes a malignant form in persons who have long been under the influence of mercury, such as miners, smelters, and workers with the metal, but experience has not at all established this. A. Kussmaul[9] stated even as early as 1861: "Although I have taken much trouble to do so, I have not been able to meet with the record of a single worker in mercury who has acquired primary or secondary syphilis whilst he was affected with mercurialism." Although we cannot speak out too positively at the present day, the syphilologists of our own times are almost unanimously agreed that mercury exerts a favourable influence in syphilis, and that there is not the slightest reason to suppose that there is any connection between the use of this drug and the tertiary forms of the disease. Thus Vajda and Paschkis (in their work on the Influence of Mercury, &c.)[10] remark: "That there is any causal relationship between mercury and later syphilitic manifestations, regard the nature of such a relationship how we may, is not to be supposed." Ullmann[11] also shows in a recent publication emanating from Professor Ludwig's laboratory, that in experiments upon animals, even after fatal chronic poisoning by the metal, it is absent from, or is only to be found in mere traces in those organs in which, according to the views of

the antimercurialists, it should be most abundantly deposited, such as the bones.

Other syphilologists, although convinced of the harmlessness of mercury in this respect, may nevertheless be divided into two sharply defined groups as regards their ideas on the relation between mercurial treatment and the development of tertiary syphilis.

According to the one party, mercurial treatment has absolutely no influence upon the general course of syphilis. The quality of the syphilitic virus, which may produce a severe or slight type of the disease, is alone held responsible for the occurrence of tertiary symptoms, and it is supposed to be possible to predict the development of tertiary lesions from the character of the early manifestations.

Thus Diday[12] found that cases treated with or without mercury were equally liable to tertiary symptoms. He distinguished (1858) a *syphilis décroissante* and a *syphilis progressive;* the first he merely treated by hygienic measures, for the latter he employed mercury and iodide in addition. In the same way he at a later period[13] emphatically asserted that mercury is not capable of preventing the occurrence of secondary symptoms, but merely imparts to them a milder character. In the year 1882 he embodied the result of a long series of observations in the following propositions:—

1. The administration of mercury from the appearance of the chancre does not prevent the development of secondary symptoms.
2. It is quite the same thing whether one commences mercurial treatment before or after the appearance of the secondary symptoms.
3. Mercury is equally ineffectual in preventing relapses.
4. He holds fast to the so-called law of concordance, and regards the tint of the earliest exanthem as of special importance, the prognosis being more unfavourable the darker its tint.
5. Syphilis is in the majority of cases a slight disease.
6. But one must nevertheless endeavour to mitigate all severe syphilitic eruptions by mercury, which drug is, however, quite impotent during the latent period.

Still later[14] he classified syphilis as follows, according to the severity of its manifestations :—

1. Syphilis which is merely indicated (*ébauchée*) (1 case in 93).
2. Mild syphilis (53 cases in 93).
3. Severe syphilis (29 cases in 93).
4. Galloping syphilis (4 cases in 93).
5. Tertiary syphilis, or the "syphilitic diathesis."

He also believes that the development of tertiary symptoms may be predicted from the primary and secondary manifestations ; if these be benign, the risk of tertiaries is reduced to a minimum, and if individuals so affected should suffer from tertiary symptoms, these are quite insignificant and benign in character.

Jullien,[15] a pupil of Diday's, in one of his earlier works, based upon statistics, arrived at the following highly remarkable results, viz., Syphilis not treated at all runs the most benign course, then come cases treated *ab initiis* with mercury, and lastly tertiary manifestations are commonest in cases treated with mercury *a secondariis*.

In his admirable text-book[16] he himself remarks later that statistics can rightly be quoted against him which prove the contrary proposition, but he does not attach any great importance to treatment in this relation. He has much more belief in the effects of other influences which may play a certain part as *causes occasionnelles* in the ætiology of tertiary syphilis, and especially of its nervous manifestations. Among such he mentions excessive brain work, venereal excesses, alcoholism, emotional disturbances, and the influence of cold, injury, &c.

H. Zeissl[17] shares for the most part the views of Diday. He embodies his experience in the following propositions :—

1. Expective treatment demands a long time (as far as the disappearance of the syphilitic symptoms are concerned), but in the great majority of instances definitely cures the disease. After such treatment relapses seldom occur, much less often than after an early mercurial course.
2. Treatment by iodine stands next to the expective plan. The preparations of iodine are efficacious in all forms and in all phases of syphilis, and even against the most severe manifestations, but its action is much slower than that of mercury.

3. Only when the syphilitic symptoms do not yield to the purely expective or iodine treatment, small doses of mercury may be employed (Littmann's decoction, or 9-12 inunctions to 2 grammes) whereby the symptoms are definitely cured.

According to C. Sigmund[18] when the primary syphilitic lesions are submitted to purely local treatment only very slight secondary manifestations develop in 40 per cent. of the cases, which are often so insignificant that they escape the notice of the patient. In 10 per cent. more distinct symptoms, but of short duration (erythema, papules), appear, which, however, recover without general treatment. Severe secondary affections do not occur with any greater frequency under a more expectant treatment than when anti-syphilitic treatment is at once resorted to. Experience rather teaches the opposite. General treatment should be only commenced in the secondary stage, and then only when several systems and organs appear to be affected by the disease, or when one is attacked with unusual severity, or lastly if the nutrition and functions of the organism are involved, obviously as the result of syphilis alone. With the milder forms local treatment suffices.

Nevertheless Sigmund remarks that in gummatous conditions mercurial inunction has a more lasting effect than treatment by iodine preparations, the action of which, although usually rapid, is but little lasting. In a word, mercury is still frequently the mainstay in the third stage of syphilis.

The transition to the tertiary stage is usually met with only when syphilis is complicated by other disorders; tertiary syphilis usually occurs only in individuals, of defective organisation, with an hereditary disposition, or who are sufferers from disease of other kinds, and in these under unfavourable conditions; whereas in well-organised individuals and under favourable hygienic conditions, they are of a benign character, and treatment does not fail to bring about the desired result.

Mauriac[19] too regards general causes, some constitutional and other external, as the chief impetus to the development of tertiary lesions. He holds all theories as to the quality of the syphilitic virus as pure hypotheses, which are neither proved by statistical data, nor have any theoretical basis. He specially points out that the law of concordance has no existence. From the primary

manifestations it is only possible to form some idea of the characters of the first eruption, but one can never arrive at any conclusion from the primary and secondary manifestations as to the further course of the disease. Much more frequently an attack of syphilis, which is at first benign, assumes suddenly, or at a later period, a malignant character.

In sharp contrast to the above view stands the notion that a relation exists between really satisfactory mercurial treatment on the one hand and the course of the syphilis on the other hand. a teaching which was inaugurated by Fournier (1874), and which in Germany has been especially upheld and emphasised by Neisser.

This view culminates in the proposition that "mercury is not merely a symptomatic drug affecting the syphilitic manifestations, but a preventive drug which attacks the syphilitic virus itself. Only by long-continued mercurial treatment are we in a position to influence the actual disease, and the chief cause of the development of the tertiary lesions is in insufficient or quite neglected mercurial treatment in the early stage. Just because the initial symptoms and early manifestations afford no insight into the further course of the disease, and indeed tertiary symptoms, and even the most dangerous ones, are especially apt to develop in the course of an attack which is at first quite mild (and usually insufficiently treated), it is necessary that all syphilis should be equally carefully treated."

Moreover, Fournier dismisses the "law of concordance" as devoid of any foundation. As already stated, Fournier adopted this standpoint of his, which also was the basis of his chronic intermittent mercurial treatment, as early as 1874.[20] Since then he has in an admirable series of works[21] continually maintained his thesis, and has been continually strengthened in this belief by the material which he has collected with the greatest perseverance. His latest results are embodied in a large collection of statistics of cases of tertiary syphilis presented to the first International Dermatological Congress at Paris, 1889, and in his admirable book on the Treatment of Syphilis.

Amongst German authors the most energetic adherent and upholder of this doctrine is Neisser, who, in 1884, collected in a complete manner all the arguments, both empirical and theoretical, which support Fournier's view, and expounded the grounds for

the necessity of long-continued intermittent mercurial treatment.[22, 23].

Unfortunately I must refrain from discussing more fully the literature of this question, and can merely state briefly that the following are among the authors who regard mercury, not as a mere symptomatic remedy, but as one which has a direct influence upon the syphilitic virus, and are therefore adherents of the chronic intermittent method of treatment, or who at least hold that treatment is desirable even in the latent periods: Ricord[24], Fournier[25], Neisser[22, 23], Mauriac[19], Leloir[26], Hutchinson[27], Martineau[29], Turati[30], Jessner[31], Finger[32], Elsenberg[33], Lesser[34], M. Bender[35], Drysdale[36], Haslund[37], Scarenzio[38], Rollet[39], Roussel[40], Vajda[41], &c., &c.

A question which I can here only refer to in passing is that of preventive treatment during the secondary incubation period. I should, however, mention that the same authors, *e.g.*, B. Schwimmer[28], who warmly uphold such preventive treatment, deny in principle the effect of mercury upon the syphilitic virus. Schwimmer is not consistent in this view, seeing that he allows a repeated mercurial course during the first year, even when no relapse occurs.

Ricord's principle already was: To do little in the treatment of syphilis is the same as doing nothing. He prescribed, during the first two years after infection, mercurial courses with intervals of four to eight weeks, so that ten months were devoted to treatment and fourteen months to intermissions.

During such period, and also as an after-cure, he recommends iodide of potassium.

Fournier's scheme of treatment is briefly as follows: A mercurial course lasting two months, followed by a month's intermission; a second mercurial course of six weeks, and then an interval of three months; a third course of the same duration, followed by a four to five months' pause; a fourth course of mercury lasting four to five weeks, a seven to eight months' interval, &c. Such treatment to be continued for at least two and up to four years.

Mauriac gives at the onset of the syphilis Sedillot's pills (9 grammes mercurial pill-mass in eighty pills), in the first week one pill daily, then for six weeks two a day, then for two months more one a day. In the second year he continues the

treatment with Van Swieten's liquor (1·0 hyd. perchlo., 100·0 alcohol, and 900 c.c. distilled water), one coffee spoonful being given daily. If new symptoms develop, the entire treatment is to be repeated. According to Mauriac, by this mode of treatment alone is visceral syphilis to be prevented.

Leloir does not commence the treatment until the secondary symptoms develop. He employs inunctions of 2 to 4 grammes of mercurial ointment daily for a fortnight, then allows an interval of a fortnight or three weeks, and so on during the first ten months, with local treatment between times. He attaches much importance to general hygienic and tonic measures.

Neisser introduced certain important modifications of Fournier's original method of treatment, in so far as he abandons internal treatment, and applies the mercury partly to the skin and partly subcutaneously, and also does not confine himself to mild courses only, but alternates the mild courses with an energetic one, the so-called "Hauptcur," at least once a year. The duration of the treatment should extend as far as to the fourth year.

On the other hand Neisser insists afresh, on every opportunity, that the treatment must always be adapted to the individuality of the patient, both as regards the nature and energy of the individual courses, the length of the intervals between them, and the duration of the treatment in general. He regards as the most important point the holding fast to the principle of long-continued but intermittent mercurial treatment.

Certainly such treatment carried out under medical supervision is not injurious to an otherwise sound individual, if care be taken to allow the necessary intervals to elapse.

As is well known, this teaching has met with very active opposition from many quarters, and the opposition has been specially directed against the therapeutical inconsistency of submitting every case of syphilis, whether at the outset it assume a mild or severe character, and whether the symptoms be present or no, to a similar energetic and chronic mercurial treatment lasting over years. Such treatment is regarded as both superfluous and injurious.

I will not omit to allude briefly to the views of a few celebrated syphilologists upon this subject.

Thus Kaposi[12] regards syphilis as an undoubtedly curable disease, and indeed as one of the most readily curable ones, yet he regards

the chronic intermittent form of treatment as unnecessary because he has seen many patients who have remained healthy after a single course, and on the other hand many others who would continually suffer from relapses in spite of frequently repeated courses. He accordingly regards it as the chief point to carry on the first treatment carefully and for a long enough period, a fresh course being called for only if characteristic syphilitic manifestations recur. He does not believe that a rationally conducted mercurial treatment is injurious to the organism, and therefore he has no objection to a several-times repeated mercurial course during the early years.

Neumann[43] considers that the advantages of chronic intermittent mercurial treatment are not raised above all doubt, and that on the other hand it has certain disadvantages, viz.:— (1) A psychological objection, since it increases the tendency to syphilophobia. (2) To certain individuals the long use of mercurial preparations is not innocuous. On the other hand, he regards the method as having an adequate theoretical basis, since he has shown that after the disappearance of the clinical manifestations, exudation cells remain for a long time both in the seat of the first lesions and also in other organs, by the increase of which relapses are caused. Nevertheless Neumann remains an adherent of the symptomatic treatment, having regard to the cases in which patients remain free from further symptoms after a single course. In the course of the last ten years he has very fully observed thirty-six such cases in his practice. Since, however, syphilis almost always recurs in the first year, and very frequently in the second, no very great difference exists, as a matter of fact, between his plan of treatment and Fournier's. Moreover, Neumann agrees that to obviate the transmission of syphilis to their posterity, syphilitic parents should be submitted to mercurial treatment, even at the period when symptoms are wanting, and also that it should be resorted to before marriage, if not more than four years have elapsed since the infection. In conclusion he adds: "Fears that by repeated use of preparations of mercury and iodine the organism may suffer, are not well grounded, provided that the treatment be conducted on suitable and scientific prineiples." "On the other hand it is true that in some instances, owing to individual peculiarities or variations of quantity, a supersaturation of the organism with mercury occurs,

in which cases there results from its continued use a failure of nutrition, and a complete loss of its influence upon the syphilitic efflorescences."

Finger[32] is indeed, as has been already mentioned, an adherent of the chronic intermittent treatment, but he does not treat the slight cases with mercury, but only with iodine.

J. Caspary[44] offers a much more active opposition than do the above-named authors. He differs completely from the views of Fournier and Neisser. He regards the use of mercury, even under careful control, as not altogether innocuous to the organism, especially when it is employed in the latent stage. He commences specific treatment only after the appearance of secondary symptoms, and only repeats it if relapses occur.

It is true that M. v. Zeissl[45] expresses the opinion, 1884, that it is not advisable to stop the treatment of syphilis as soon as the symptoms have disappeared, but that the treatment must be persevered with for a long time, at least for a year; however, he employs iodine preparations for this purpose, which preparations we regard as absolutely valueless in the treatment of the virulent stages. At the most he allows, when manifest symptoms are present, and if the patient has an undue confidence in mercury, a short course of inunction. He regards it, however, as not advisable to administer mercurial preparations for a long time. (*e.g.*, four to five years). His plan of treatment, which corresponds with the traditions of the school of H. Zeissl, is as follows[46]: Before the development of general symptoms the primary lesion is to be treated topically. On the appearance of the earliest general symptoms (roseola, papular syphilide, or broken down papules on the mucous membranes), no anti-syphilitic treatment is for the time being to be adopted, but the involution of the manifestations is to be sought by means of dietetic measures, local treatment, &c. If this does not result within eight weeks, he gives iodide of potassium. If the symptoms have still not disappeared in eight weeks more—and even if they have already disappeared—resort may be had to mercurial treatment (by Zittmann's decoction or inunctions), and afterwards iodide is to be continued for a period of at least six months to a year, even when relapses occur. Only if this prove useless mercury may be resorted to (ten to twelve inunctions), since "we know from the experiments of Helva and H. Zeissl that mercurial inunctions in

considerable numbers are borne by healthy individuals without ill effects."[47]

Lassar[48] too is an adherent of the symptomatic treatment, but he permits a precautionary course before marriage, even when there are no symptoms present. As regards his views on tertiary syphilis,[30] I shall come back to his statistical observations later. He emphasises the value of iodide of potassium, but nevertheless holds that in late syphilis a course of iodide combined with mercury is much more sure in its effects than iodide alone.

E. Lang[49] is also an opponent of the chronic intermittent treatment. According to him, facts do not sufficiently prove the correctness of Fournier's views, since he also has found that very often relapses have continued to occur in spite of energetic treatment by mercury and iodide.

He is therefore convinced that better results are often to be obtained by a more expectant attitude than by energetic treatment. He follows indeed the "golden middle course," and lays the chief stress upon local, and when it is applicable, on regional treatment. When the disease has once become constitutional, he takes the direction of further treatment from the nature of the syphilitic effects. Symptoms which are not annoying, which lead to no destruction or disfiguration, and do not involve any risk of infection to those around the patient, are to be quietly left to spontaneous resolution. He would therefore not attribute a dereliction of duty to any one who did not treat a roseola. Even isolated papules do not call for any general treatment. Only if a widely distributed papular rash appears is such treatment called for, or speaking generally if the syphilitic affection attains to importance by the great number of its resultant lesions; by its localisation in important organs; by a tendency to softening and suppuration, &c. The length of time during which the treatment is to be pursued always depends upon the severity of the process, but in any case it is advisable to carry it on for some time after the complete disappearance of the symptoms. With mercury, however, and especially with inunctions and injections of grey oil—an excess administration for one week should suffice. An exception is only to be made where there is a danger of transmission of syphilis to offspring, and then the treatment should be carried

out even if no symptoms are present. Under such circumstances excess is always better than too little treatment.

Von Watraszewski[50] is no adherent of mercurial treatment in the latent period, and regards Fournier's method as incorrect.

Köbner sharply attacks Fournier and Neisser, and condemns the chronic intermittent mercurial treatment as capable of producing severe nervous symptoms and gastric disturbances. He also states that according to Neisser energetic treatment with insoluble salts should be carried on for seven years!* He lays special stress upon the importance of hygienic measures and regional mercurial treatment.

I must here also mention that Diday,[52] in a publication which has very recently appeared, assails Fournier very energetically, and believes that he has drawn erroneous conclusions from his statistics.

Quite recently also Lang[70] has raised strong objections to the arguments of Fournier, into which objections we shall have to enter more fully in the special discussion.

If we submit the works quoted to a brief criticism, we shall see that only some of the above authors are directly opposed to our view, since, strictly speaking, most of them start as we do with the view that mercury is capable of exercising a direct influence upon the syphilitic virus. What other inference can be drawn from the fact that they treat syphilitic patients with mercury in consideration of transmission, marriage, and pregnancy, even when all symptoms are wanting at the time? But if under such circumstances advantage is taken of the preventive action of mercury, is it not a mere logical postulate that the patients themselves, apart from the interests of any third person,

*It is unfortunate that Köbner has not stated which communication of Neisser's he had in view in this quotation, since Professor Neisser has authorised me to state that he has never maintained that the treatment should be carried on for seven years, and still less that insoluble salts are alone to be employed. He merely says (Ueber Therapie der Syphilis Verhandl. des v. Congr. für innere Med., 1886, p. 32) that special importance is to be attached to the primary course, for which one employs either a well-performed and long-continued inunction course, or injections of insoluble mercurial salts to which he attributes an equal value. Beyond this a single similar main course should be carried out in the first, second, third, and, if possible, in the fourth year, and in addition to this main course, milder courses (injections of easily soluble mercury salts, or internal administration of mercurial preparations) are to be resorted to during the first and second years. I cannot, therefore, discover from whence Köbner has obtained the data for this charge of his.

should be subjected to similar prophylactic treatment? What is the significance of the recommendation which they almost all repeat that "the first course should be specially energetic, and should, moreover, be extended beyond the duration of the symptoms"? Is not the idea here also expressed that one wishes to attack the virus? If, however, one holds this view, why does it not hold good for all the years during which we speak of all our patients as not cured, but as being simply free from symptoms, during which for example we forbid them to marry? Especially since most of them confirm the statement that mercurial courses carried out with proper precautions do not involve any risk to the patient, provided that care is taken to allow the necessary intermissions; and I may add that such risk is better avoided in our treatment, which is essentially intermittent, than is often the case under purely symptomatic treatment. Under such treatment it much more often happens that very large quantities of mercury are introduced into the patient in a comparatively short time, as for instance when in obstinate cases relapses occur in quick succession.

We endeavour to preserve the necessary intermissions under all circumstances, with the exception of actually menacing cases, and do not allow ourselves to be put off from waiting by harmless symptoms. Naturally we too have failures, but one should not be led to pronounce a condemnatory judgment on the strength of quite a few unfavourable results. What are we to think when, for example, M. v. Zeissl[53] submits two patients in all to the chronic intermittent treatment, and because unfavourable results were obtained in both cases will have nothing to do with the whole method. Moreover, if we examine these two cases, we find that we have not in them an intermittent treatment in the sense of Fournier and Neisser. In the first case the patient was treated on the expectant plan for four weeks after the eruption of a maculo-papular syphilide, for four more weeks he took iodide of potassium, and only when the rash had already nearly disappeared thirty inunctions of 2 grammes, and only six months later thirty inunctions of 3 grammes each were administered. The second case was treated in just the same way at the outset. Quite apart from the fact that the first course consisted of only thirty inunctions of 2 grammes each, which can certainly not be regarded as a thorough first course, even this course was only

initiated some months after the appearance of the secondary symptoms.

We, however, expressly insist that a very great importance attaches to the first treatment, which should not only be very energetically and carefully carried out, but also in good time, indeed as early as possible.

Neisser has stated on theoretical grounds that it is best to begin the mercurial treatment as early as possible, before the development of secondary symptoms indeed (but only after the diagnosis of syphilis has been surely established).

He has not, however (for example in his paper read at Wiesbaden), taken up any practical standpoint on the question, but of recent years he has constantly (when the diagnosis is certain) commenced the preventive early treatment before the appearance of secondary manifestations. If, on the contrary, a patient has been without mercurial treatment for months at this very stage, which is a most important one, one may certainly assume an unfavourable influence of such so-called "expective treatment" upon the whole course of the disease, a deposition and implantation of the virus in the tissues, which can surely only render its subsequent elimination more difficult. At any rate, I believe that many cases in the statistics certainly indicate that a delayed mercurial course has no longer so favourable an action, simply because it has been commenced many months after infection. At least such cases are not strictly suitable to be employed for the estimation of the value of the chronic intermittent treatment.

Most of the opponents of this plan of treatment start from contrasted observations. They say, we have watched such and such a number of cases for years together, and the patients, although they had only undergone a single mercurial course, have remained healthy. On the other hand, we have cases in which, in spite of energetic treatment, relapse after relapse occurred, and in the end even tertiary symptoms were suffered from.

That both statements are correct goes without saying; we have observed the same. The question then arises, how far such more subjective impressions, which for the most part are not represented in figures, have an objective value? Undoubtedly the solution of this problem is only to be brought

nearer by a large mass of statistics, but I fear that we shall have long to wait for a truly conclusive set of statistics* with hundreds of cases on both sides treated by Fournier's and Neisser's method and on the expective plan respectively.

The value of isolated observations is so much the less because a few unfavourable cases naturally always cleave more to the memory than the many favourable ones which we have seen for a short time, and which we do not see again, because they remain well for years together.

Is it the case, however, that these cases, so benign at the onset, have always remained so benign?

It seems to be established, on the contrary, that cases which are very benign at the commencement, and which under symptomatic treatment seldom undergo more than a single course, form the chief contingent of the tertiary cases (and especially of late developing nerve-syphilis), even if there are on the other hand truly benign cases which run a favourable course apart from long-continued treatment.

But does one know at the beginning which these benign cases are? We hold that, seeing that any assurance for the future of a case of syphilis, however benign at its commencement, is wanting, we are bound to treat all cases alike, even in view of the possibility of treating many superfluously.

* Ideal statistics of this kind should include a very large number of thoroughly observed cases of syphilis, in order to ascertain how many are cured by a given plan of treatment and how many have gone on to the tertiary stage. In the nature of things, however, the presentation of such statistics is simply impossible, seeing that experience shows that tertiary lesions may develop 25 to 30 years, or even longer, after infection, and it is necessary to watch the syphilitic patient to the actual end of his life, or at least for several decades. But where has anyone such a material at his disposal?

Hundreds of our cases disappear entirely from our view, others die from undiagnosed syphilitic visceral lesions and so are missing from our tables, and so on. Neisser has called attention to all these difficulties, and accordingly at the fifth Congress for Internal Medicine at Wiesbaden he suggested preparing the way for safe statistics by a kind of collective investigation, which should not confine itself to the arrangement of the material at present to hand, but which by a species of collective work upon mutual principles should conduct the treatment of syphilis during the coming years and decades according to certain concordant principles, and so furnish a supply of good and long-observed material as the basis of really useful statistics.

Köbner afterwards took up this idea. Tables were prepared by Köbner and Neisser in association, which should form the basis of the morbid histories, but only very few clinics and still fewer practitioners have taken any notice of this suggestion.

We are convinced that by so doing we protect a considerable number of our patients from tertiary lesions.

I must repeatedly insist, in this connection, that such chronic intermittent treatment, and even Neisser's energetic mercurial treatment, when rationally carried out, is not attended by any danger to the organism. Neither Prof. Neisser (whom I have consulted on this special point also) nor I myself have observed any injurious effects. We are quite unable to agree with the statement that patients submitted to the prolonged treatment "not infrequently waste, suffer from digestive disturbances and sleeplessness, but are most frequently affected by manifold disturbances in the domain of the nervous system."

On the contrary, we may believe that for very many patients the consciousness of being under treatment has an important influence even in the successful cure of the disease. We meet with neurasthenia, syphilophobia, and the like, certainly less frequently than do those who follow the expective plan.

We shall hardly be regarded as such bad practitioners that we shall be credited with blindly following a principle irrespective of individual peculiarities, and leave out of consideration the constitution, nutrition, and so on, of our patients.

Is there then any proof that mercury is really a specific against the syphilitic virus in the Fournier and Neisser sense?

A direct proof is afforded (and here I am in complete accord with Neisser) by the effect of mercury on the capability of transmission of syphilis. As far as we know at present it must be taken as certain that the transmission to offspring is absolutely independent of the manifestations of the disease, and may occur apart from any manifest symptoms either in the genital organs or in the organism as a whole. This very power of transmission is beyond all other symptoms influenced and abolished by mercurial treatment. This remedial working applies to all varieties of so-called transmission, both to true transmission in the stricter sense, by semen and ovum, and to the transmission of syphilis from the mother to a healthy embryo attacked during its development, whether the mother has been infected before or after conception. In all these cases mercurial treatment exercises a sure action, even with persons who for many years have had no symptoms of syphilis, both upon the fœtus itself and also upon the course of pregnancy in

syphilitic mothers. In such cases we can only be dealing with a direct effect of mercury upon the syphilitic virus. This effect clearly manifests itself even after a single energetic mercurial treatment, so that after a series of abortions, miscarriages, or premature births, which are for the most part due to latent syphilis in the father or mother, after a single energetic course to one or the other a series of normal pregnancies and healthy children follow. Still more convincing are the cases in which the antisyphilitic mercurial treatment only temporarily influences the transmission of the disease, so that only the child born next after the course can be regarded as healthy. If the treatment be not repeated abortions again occur, but if the parents be again treated a healthy child again follows.

This is most admirably illustrated by the following case, observed by Fuhrmann and quoted by Fournier[54]:—

A hitherto untreated syphilitic woman passed through seven pregnancies, with seven syphilitic children, which quickly died. During the eighth and ninth pregnancies mercurial treatment, and on both occasions healthy full-time children. She regarded herself as cured and did not submit to treatment during the tenth pregnancy; again a syphilitic child, which died at the age of six months. Repeated treatment during the eleventh pregnancy and again a healthy child.

The same is proved by large statistics as to the mortality of children with inherited syphilis, *e.g.*, one of Fournier's tables:—

	Transmission from the father.	Transmission mixed.
Treatment, none	59 per cent.	82 per cent.
,, of short duration	36 ,,	85 ,,
,, of medium duration ...	21 ,,	36 ,,
,, of long duration	3 ,,	

In some further statistics of Fournier's, of 14 absolutely untreated syphilitic men, some of whom infected their wives, whereas others did not, and who became fathers on 45 occasions, the following were the results of the pregnancies:—

Surviving children (seven of whom were syphilitic)	8
Abortions and still births	29
Children who died shortly after their birth	8
	45

or 37 deaths out of 45 pregnancies, a mortality of no less than 82 per cent.

According to the statistics of Etienne the children of untreated syphilitic mothers show a mortality of 95 per cent. (death shortly after birth in 76 per cent.), whereas among mothers who are treated it is only 11 to 16 per cent.

These figures certainly call for no further comment; they speak for themselves. A further confirmation of the preventive action of mercury is seen in the fact, which is open to proof, that syphilis in general, when left to itself and untreated, exhibits tertiary manifestations of a conspicuously more unfavourable course. To these forms belong the formerly so enigmatic diseases which occur in an endemic manner in a variety of countries, known as the Radesyge of Norway, the Skerljevo of Dalmatia, the Scotch Sibbens, the Morbus Dithmarsicus of Holstein, the Frenja of Servia, and a variety of other names, of which we now know, thanks to the investigations of Hebra, Sigmund, Neumann, Boeck, Danielsen, Genters, Pericic, M. von Zeissl, and others, that they are nothing else than tertiary syphilitic troubles, neglected, untreated, and left to themselves for years together.

To this group also belong the syphilitic-epidemics which still rage in many provinces of Russia, and which exhibit a very conspicuous variety of tertiary forms.

But even amongst ourselves the groups of treated and untreated cases are sharply contrasted, and the total number of all (tertiary) cases of so-called syphilis hereditaria tarda consist of untreated tertiary cases. Most of our tertiary clinical cases come not from the town of Breslau but from the province of Silesia or Posen and the neighbouring Poland. And this leads us to the most important point in our work, namely, to the statistics of tertiary syphilis and the importance of their bearings upon the problem under discussion.

In my opinion, allowing for all scepticism as to the value of statistical proof, these statistics allow of no other conclusion than that the greatest importance attaches to the treatment in the early period in connection with the aetiology of tertiary syphilis, and that the chief cause of tertiary manifestations is to be sought in a complete neglect or insufficient application of mercurial treatment at the commencement, seeing that *all* statistics show, for *all* countries equally, that the incomparably greater number of patients with tertiary syphilis come from among those persons

who have undergone no or only superficial mercurial treatment during the early period.

Many will, no doubt, deny absolutely the value of such "tertiary" statistics, and will perceive in such retrospective figures an actual logical fallacy. They demand a direct comparison of patients treated by the several methods in order to establish which method is the best. That statistics of this kind would be better, and indeed would alone be conclusive, we have already pointed out, but we have also shown the enormous difficulties in the way of satisfying this wish, which we most cordially share.

Is then the method which we have selected, viz., to examine a large number of tertiary cases, and to establish the cause of the occurrence of the tertiary symptoms by carefully obtaining their history, so altogether inapplicable for our limited enquiry?

We cannot, of course, thus establish the frequency of tertiary syphilis in general in comparison with the total incidence of the disease, nor useful points as regards its localisation in the several organs; but, nevertheless, the survey of a very large number of well-observed tertiary cases gives, in my opinion, very interesting and valuable data, when as regards a single question such enormous differences uniformly present themselves, as actually exist between cases of syphilis badly treated or untreated on the one hand, and treated on the other.

Of course any method of treatment one chooses cannot be picked out and made the object of statistical investigation, but only one of which we know by experience of other kinds (*e.g.*, influence on transmission or symptomatic effects), that *a priori* it may possibly exercise a preventive influence upon the event of the disease, and a direct effect upon the virus. The investigation which we are justified in undertaking in respect to the action of mercury cannot be undertaken with regard to iodine preparations, as Lang, for example, does in his critique of Fournier's statistics.

But, in my opinion, Lang makes also the following mistake. He says that if only 217 cases in 1,703 were quite untreated, whereas 1,112 were treated for a short time, Fournier is bound to draw the conclusion that, as regards tertiary developments, no treatment at all is better than a short period of treatment. But he forgets entirely that this conclusion is not to be drawn from the absolute number of untreated cases in these statistics, but

from the number of syphilitic cases generally which are untreated. This figure is unfortunately not obtainable; but in Paris it is certainly much lower than in other large cities, and still more so than in small towns and in the country. Hence, naturally, the number of totally untreated cases occupies an insignificant place in Fournier's statistics. If, however, Lang had massed together the patients with poor and moderate treatment he would have found that this amounted to 1,379, as against 324 adequately and thoroughly treated. In the same way, again, one is not justified in gathering from Fournier's statistics of cerebral syphilis that treatment by iodides has a prophylactic importance, because only 5 cases so treated developed tertiary symptoms. Since we may safely presume that only very few patients are treated with iodide alone in the early stage, and that the small number of patients so treated among those with cerebral syphilis is to be explained by the fact that they are so few in all.

The last objection which I would raise to Lang's argument is this: Lang concludes that Fournier in his statistics must necessarily as years went on have been led to alterations in the arrangement of the figures corresponding to his several groups, since he has altered his ideas of "prolonged" treatment. But here Lang overlooks the fact that Fournier has made his statistics "retrospective"; that the cases from which they are constructed were only in very small part treated by him from the first, and that he was therefore able to group the cases according to his point of view at the moment, as indeed he did.

If, however, one must declare these objections to be unfounded, one objection certainly remains well grounded, and that is the following: We divide, in our statistics, the patients with tertiary symptoms into groups according to the extent of their treatment and compare these groups with each other, without possessing corresponding statistics—that is to say, based upon treatment—of syphilitic cases of the same duration, without tertiary developments. It may be, indeed, that the relation of wholly untreated and well-treated cases is the same among the tertiary patients as among those who have remained in good health. In this case there would be no evidence of the effect of mercurial treatment upon the occurrence of tertiary symptoms.

A second way of arriving at absolute certainty would be by knowing the totals of the individual groups of syphilitic patients

treated by various methods from which the tertiary cases were derived, the proportion of tertiary to non-tertiary cases in each therapeutic category would then permit of judgment as to the value of each treatment. Unfortunately, as we well know, we must be content to want such mathematical proof. Nevertheless, we consider that we may attach a certain value to the existing statistics.

Among those hitherto published, Fournier's take the first place.[57] They embrace 2,395 cases of tertiary syphilis, all derived from his city practice.

With regard to the time after infection at which tertiary symptoms develop, his results are as follows :—(1) The frequency of tertiary symptoms increases conspicuously from the first to the third year. (2) It reaches its maximum in the third year. (3) Thereafter it decreases continuously and conspicuously up to the eleventh year, but the number of tertiary lesions is still considerable. (4) During the succeeding ten years there is still a continuous decrease, but not so rapid a one as previously. (5) Between the twenty-first and thirtieth year the numbers remain at about the same height, but during this period tertiary manifestations are already somewhat rare. (6) Lastly, after 30 years tertiary syphilis is so rare that it is rather a pathological curiosity.

The maximum of all cases falls, as already mentioned, on the earliest years after infection. Thus Fournier observed 106 cases of 129 different affections in the earliest years. Certainly some of these cases were examples of syphilis maligna præcox. Fournier himself says that such cases should not by rights be included in the statistics; and Neisser excludes this category from tertiary gummatous syphilis.

As regards the influence of mercurial treatment in the early period, Fournier states that among 100 cases of tertiary cerebral syphilis 5 only were seriously and for a long period subject to mercurial treatment in the initial stage. A further set of his statistics bearing upon this point brings out the following data :—

Among 1,703 cases of tertiary syphilis there was administered in the early period,

No mercurial treatment at all	in	217 cases
Quite short mercurial treatment (under 1 year)	in	1,162 ,,
Moderately long treatment (1—2 years)	in	265 ,,
Long (over 2 years)	in	53 ,,
Treatment extending over at least 3 years ...	in	6 ,,
		1,703 ,,

In 59 cases only was the treatment adequate, and in 1,644 cases it was either altogether wanting or was insufficient. This corresponds to a percentage of 3·4 per cent., and in only 0·35 per cent. (six in 1,703) was the treatment continued during three years.

In addition to insufficient mercurial treatment, alcoholism is, according to Fournier, to be included as an ætiological factor, especially in syphilitic nervous affections. As a rule alcoholic excesses favour the development of tertiary manifestations. As to the frequency of tertiary lesions of the several organs, those of the nervous system occupy, according to Fournier, the first place, constituting, according to him, a third of all tertiary affections (1,058 in 3,721); then follow skin affections (787), subcutaneous gummata (428), affections of bones, mucous membranes, &c.

Neumann's[59] results, which he presented in part at the first, and in part at the second, International Dermatological Congress, are as follows:—

Among 9,742 cases of syphilis which he observed in his clinic, 665, or 6·82 per cent. manifested tertiary symptoms.

The chief causes of tertiary syphilis are the complete absence or insufficiency of treatment in the recent stage, and moreover constitutional diseases, such as tuberculosis, malaria, scurvy, diabetes, Bright's disease, and chronic alcoholism.

Tertiary syphilis is not merely to be regarded as metastatic, but is in most cases the product of exudation-rests remaining behind in the tissues, which, as a result of the above-mentioned causes, undergo renewed proliferation.

Tertiary syphilis most frequently appears in the third year after infection, the skin is most frequently attacked, and then the mucous membranes and bones. Endemic syphilis constitutes no disease *sui generis*, but is an ordinary tertiary syphilis, including a few cases of syphilis hereditaria tarda.

Haslund's statistics[60] (laid before the first International Dermatological Congress in Paris, and the tenth International Medical Congress in Berlin) supply the following data:—Among 5,636 cases of constitutional syphilis which Haslund treated at the Communal Hospital in Copenhagen, between 1882 and 1889, were 616 cases of tertiary syphilis, constituting 10·9 per cent., including 349 males (11·6 per cent.) and 267 females

(10·5 per cent.). These cases he divides into three groups as follows :—

(*a*) Those who had undergone no previous treatment at all.

(*b*) Those who were incompletely treated with mercury, *i.e.*, only for a short period in the secondary stage.

(*c*) Those in which the treatment in the secondary stage apparently left nothing to be desired.

The groups *a* and *c* included 94 and 208 males respectively, and 95 and 137 females, or 86·7 per cent. of the males, and 86·8 per cent. of the females.

We are confronted, almost with the inflexibility of a law of nature, by the fact that neglected or inadequate treatment of secondary syphilis leads at a later period to tertiary developments.

The group *c*, consisting of cases which had apparently been well treated, included 47 males and 35 females, but in most of these cases ætiological factors could be traced, such as alcoholism, other diseases, too late commencement of treatment, infection at an advanced age, and in 15 cases only Haslund was unable to find any explanation of the occurrence of tertiary affections.

He gives the following as predisposing causes of tertiary syphilis :—

1. Complete absence of treatment in the secondary stage.
2. Inadequate or incomplete treatment during the same period, whether of too short duration or commenced too late. The above two causes are the most important and most significant.
3. Alcoholism.
4. Other chronic diseases.
5. Infection at an advanced age.
6. Lowering of the resistance of the organism.
7. Infection in another zone.
8. Malaria or climatic fevers.
9. Idiosyncrasy, or intolerance of mercury.

As regards the frequency with which different organs are attacked, Haslund found affections of the skin in 343 cases, of the osseous system in 165, of the nervous system in 163, of the mucous membranes in 120, and of internal organs in 27 cases.

At the Berlin Congress, Haslund did not enter upon the questions of age and of the period between infection and tertiary

developments, but at the Congress in Paris he brought forward the following data.

In males most cases occurred between the twenty-fifth and fortieth year, in females between the twentieth and fortieth (women usually acquire syphilis earlier than men).

Tertiary lesions most frequently appear during the first twelve years after infection, but nevertheless they frequently develop in the first year. Among 290 males, Haslund met with 23, and among 224 females, 16, who were attacked with tertiary manifestations during the first year after infection.

According to Drysdale[61] tertiary cases constitute about 8 per cent. of all cases of syphilis; he also regards want of mercurial treatment during the secondary period as the main factor in the causation of tertiary syphilis, and therefore, seeing that one cannot be at all sure which are tertiary cases, he treats all cases of syphilis alike with mercury.

According to Mauriac[62] tertiary syphilis occurs in 10 to 20 per cent. of the cases, and as regards the period after infection at which tertiary manifestations occur, Mauriac holds that this covers, on the average, 3 to 6 years; but such lesions may occur, on the one hand, even in the first year, and frequently during the first months, and on the other hand, 40 years or even longer after infection. The most frequent tertiary manifestations are those of the skin, mucous membranes, and subcutaneous cellular tissue, which constitutes about 50 per cent. of all tertiary lesions. The most important of the visceral lesions is syphilis of the central nervous system, seeing that this is most to be feared after an attack which at the outset is of a very benign character, and visceral syphilis is an exception in the malignant form of the disease. Visceral syphilis can only be guarded against by chronic mercurial treatment.

That bad hygienic conditions, physical and moral evils, excesses, dyscrasias, poisonings, and, in short, any influences which have a weakening effect upon the organism, may favour the development of tertiary affections, and that predisposition also plays a certain part is, according to Mauriac, undeniable, but the occurrence of tertiary syphilis is always a matter of chance.

Vajda[63] found amongst the patients of the Vienna General Hospital between 1868-77, among 9,739 cases of syphilis, 632 or 6·8 per cent. tertiary cases, but he holds that this number is

about one-fifth too low. However, only 267 cases were available for statistics. Among these there were 62 per cent. previously quite untreated. Of the remaining 38 per cent. he could only ascertain the previous treatment in half the cases. In 23 cases mercury, in 12 iodide, and in 10 iodide and mercury, had been employed. Patients previously untreated manifested tertiary symptoms on an average after three years and seven months, whilst those previously treated only after seven years and four months on an average. In a word, tertiary lesions developed twice as quickly in untreated as in treated cases.

Among 166 untreated cases severe affections occurred in 143, and among 101 treated cases, in 52 only.

The majority of cases of tertiary syphilis occur between the twenty-eighth and fortieth years of life. Among other diseases tubercle, alcoholism, and malaria exert an influence upon the development of tertiary lesions.

The weight of tertiary syphilitic patients is on the average about ten kilogrammes, or less than that of healthy individuals. According to Vajda also, tertiary syphilis is especially a disease of weakly individuals.

Leloir[64] also holds that tertiary syphilis very frequently develops as early as the first year, and even in the first months after infection, but is most frequent in about the third year of the disease. The chronological division into secondary and tertiary stages is therefore incorrect, since the occurrence of tertiary symptoms is not limited to any special period. We should speak of "non-destructive resolving syphilomata," or of "erythematous lesions" (the second stage) and of "destructive non-resolving syphilomata" (the third stage).

The initial symptoms afford no criterion of the later course of the disease, and a large number of the most severe tertiary symptoms actually follow mild initial symptoms.

Lassar[65] states that among 200 cases of tertiary cutaneous lesions which he observed during the two first years, histories were entirely wanting in 60, although the diagnostically conclusive results of specific treatment were never wanting.

Quite recently there has appeared the work of J. V. Hjelmann,[66] which is concerned with the ætiology of tertiary, and especially of cerebral syphilis.

Exclusive of cases of tabes and of paralysis, Hjelmann

observed (between the years 1878 to 1890) 1,860 cases of tertiary syphilis affecting the various organs in the following proportions :—

Skin	985
Osseous tissues	238
Bones of nose and hard palate...	223
Soft palate	318
Larynx and trachea	93
Genital organs	50
Testicles	32
Nervous system : brain	218
Brain and spinal cord	12
Spinal cord	24
Other nervous affections	2

Twelve per cent. of all the cases coming under the head of syphilis of the nervous system.

Hjelmann holds that cerebral syphilis develops in more than a quarter of the cases within the first year, and in about a half of the cases in the earliest years. Thus among 112 cases of cerebral syphilis he met with 24 in which the lesions appeared between the first or second years, and 14 developed between second and third years. The period between the infection and the appearance of cerebral syphilis is shorter the later the age at which the affection has occurred.

The majority (82 to 88 per cent.) of those suffering from cerebral syphilis had undergone either no treatment, or at any rate a very inadequate treatment, before the occurrence of the tertiary symptoms.

Severe brain work, mental emotions, injuries, venereal excesses, and above all alcoholism (at least 30 per cent.) also constitute predisposing causes of cerebral syphilis. The prognosis is moderately unfavourable (30 per cent. mortality), and cerebral syphilis, without mercurial treatment, has always a deleterious effect; but the result of an early commenced and very long maintained mercurial treatment is to bring about recovery in 24 per cent., and improvement in 25 per cent.

It will be seen then that all these investigators agree in thinking that the chief cause of tertiary syphilis is to be sought in the omission or insufficiency of mercurial treatment in the early period.

They also show that tertiary syphilis develops even moderately soon after infection, and is indeed much commoner in the

first years after infection than has hitherto been generally supposed, the maximum falling at about the third year. I too can confirm this from my statistics, as regards which I may emphasise the fact that cases of malignant "galloping" syphilis (with acute multiple ulcers) are not included, because I believe that such cases must be separated from those of tertiary syphilis.

Yet I must adduce two further objections to the greater number of the preceding statistics.

I must protest, in the first place, against the inclusion of tabes and paralysis among the tertiary syphilitic lesions of the nervous system.

Secondly, against the indiscriminate inclusion of all cases of cerebral and visceral syphilis in the category of tertiary syphilis.

As regards the first objection: I cannot here enter more fully into the exceedingly difficult question of the connection between syphilis on the one hand and tabes and paralysis on the other. That such a connection exists is beyond question, after the very remarkable statistics of Erb, Fournier, and their adherents. However, it still remains an open question in what manner syphilis is an ætiological factor for tabes and paralysis, and we are certainly not justified in regarding all cases of tabes and paralysis as available for statistics of tertiary syphilis, especially whilst converse statistics still require to be made to show whether syphilis is actually a factor (direct or indirect) in the causation of these nervous affections.

It is equally difficult to accept Strümpell's toxine hypothesis, to which Neisser has rightly objected by asking why then tabes is not caused by the toxine at the period when this must be present in the body in the greatest abundance, namely, in the most recent stages of syphilis, but as a rule only in the later years after infection.

We must then leave aside from the statistics the cases of tabes and of paralysis.

As regards the second objection: it is a fundamental error, as Neisser has already pointed out, for authors to reckon all cases of visceral and cerebral syphilis as obviously tertiary.

No doubt all affections of this kind occurring in the later years are with few exceptions to be included in this category, and we know from post-mortem observation and microscopic examina-

tions that we have in such cases to do with gummatous degenerated or degenerating growth in the meninges, vessel-walls, &c. There is, however, no reason why there should not exist in the cerebral vessels, &c., the same remarkable differences between early and later, between secondary and tertiary lesions, as in the skin, bones, &c. Why do we here discard a differentiation which we draw very sharply in the cases of visible syphilitic lesions.

May we not assume *a priori* that the same papular forms are developed in the internal organs also. The more so since we know that in the early stages of syphilis the whole organism is permeated by the virus. It is true that it is difficult to establish microscopically a distinction between secondary and tertiary changes, but from the clinical and therapeutical standpoint such a distinction exists; in the latter respect in the fact that iodine preparations only have a conspicuous effect upon tertiary gummatous lesions, whereas in secondary lesions mercury is indispensable. If one has gradually become accustomed to treat cases of cerebral syphilis by the "combined" method, because, on the whole, one has seen better results from it, this is not only because of the undoubtedly useful aid afforded by mercury in tertiary cases, but also because mercury alone has a curative influence upon secondary cerebral affections, to the cure of which the iodine preparations do not contribute in the least.

Having regard to these two points, the scale of frequency in the tables of localisations undergoes a conspicuous amount of shifting, and the fact, for example, that Fournier places tertiary lesions of the nervous system so high, and assigns to them the first place in his statistics (with indeed a much larger number of cases than of affections of any other organ), whereas the data embodied in other statistics agree in assigning the first place to skin affections, appears in quite a different light. After Fournier it is Haslund who gives the largest figures for syphilis of the nervous system. In his statistics it takes the third place with a total of 163 cases, but as against this figure he has 343 cases of cutaneous lesions.

Haslund seeks to explain the great difference between his results and Fournier's by the fact that his material is derived from hospital patients, who mostly come from the working classes, whereas Fournier's were private patients belonging to

higher social strata ; one must suppose that among such people tertiary syphilis of the nervous system is of more frequent occurrence.

I am prepared to agree with Haslund that differences in the classes from which the patients are derived, and perhaps national peculiarities also, play a certain *rôle*.

How great is the difference in this respect between private and hospital patients is sufficiently evident from my statistics, in which the number of cases of nervous affections among the first class far exceeds that in the second, a point to which I shall again have to refer later. That various countries, and even various parts of the same country, show different percentages of tertiary syphilis is a known fact; and, lastly, it is conceivable that in France patients with syphilis of the nervous system consult the syphilologist more often than the neurologist, and, above all, consult Fournier in his double capacity as syphilitic and nerve specialist.

Moreover, Fournier has in his statistics separated 428 cases of gummata of the subcutaneous tissues from the tertiary skin affections, and these two groups, which are certainly hard to distinguish from each other, would, if combined, have taken the first place. The same holds good, for the most part, for the group of "tertiary syphilides of the genitalia," amongst which 157 cases are separated off and classed in the great group of syphilides of the mucous membranes. Many of these might certainly be reckoned, without stretching a point, among skin affections. These two factors which have been referred to, viz., 1, the question of localisation in general, and 2, the differences between hospital and private practice, afford, in my opinion, a sufficient explanation of the difference between Haslund and Fournier's data.

Since, however, in Haslund's statistics, which deal exclusively with hospital patients, tertiary nervous affections reach a very high figure in comparison with other hospital statistics, and especially with my own, and seeing that Haslund makes no mention of tabes and paralysis I must assume that he has included these also in his statistics.

Our statistics embrace the cases of tertiary syphilis which come under observation in the Royal Dermatological Clinic and Policlinic in Breslau during the period 1882 to 1892, as well as

the private cases observed by Prof. Neisser during the same period, and by myself during the past nine years.

I may state at the outset that I have only included those cases in which full and sufficient data were forthcoming as to whether, and in what manner, mercurial treatment was carried out in the early period. The cases of which I have made use are also, as regards the early treatment, quite reliable and certain.

I have not included in the statistics cases of syphilis maligna præcox. Whatever view one may take as to the significance and ætiology of this variety does not here concern us, since in such cases even the earliest general eruption, even before any treatment is employed, manifests an ulcerative tendency. For my own part, however, I share on these points Neisser's view, that the gummatous and acute ulcerative forms are totally different processes.

I have investigated with special care those cases in which, after a quite normal early course, true gummatous lesions have sometimes developed as early as a few months after infection. In such cases one almost always finds that either there has been no treatment at all (and this is more commonly the case), or that treatment has been commenced too late. I have also paid special attention to those cases in which the syphilis has suddenly taken an unfavourable direction, frequently in spite of even very energetic mercurial treatment.

Our statistics (which have unfortunately been much reduced by this vigorous sifting) embrace 673 cases of tertiary syphilis in all, 319 of which are cases from the clinic and polyclinic, 244 from the private material of Prof. Neisser, and 110 cases from my own private practice.

As already mentioned, I have grouped the two sets of statistics (from hospital and private patients) independently of each other, and they are set out here, for purposes of ready comparison, in the two following tables.

We will test the results of the two tables and subject them to criticism.

I. In the first place, it is seen that among the hospital patients the number of females suffering from tertiary syphilis is larger than that of males—54·6 per cent., 45·4 per cent. This is, however, in nowise due to a greater frequency of the occurrence

TABLE I.—HOSPITAL IN-AND-OUT-PATIENT MATERIAL.

319* cases, including 145 Males (45·4 °/₀) and 174 Females (54·6 °/₀), amongst whom were 22 girls (12·6 °/₀).

Age.	1—10.	10—20.	20—30.	30—40.	40—50.	50—60.	60—70.	Over 70.
138 Males	—	6 4·3 °/₀	45 32·6 °/₀	43 31·1 °/₀	26 18·8 °/₀	16 11·6 °/₀	2 1·5 °/₀	—
182 Females	1 0·6 °/₀	8 4·7 °/₀	39 24·6 °/₀	63 38·7 °/₀	30 19·1 °/₀	15 9·1 °/₀	5 3 °/₀	1 0·6 °/₀

Period after Infection at which Tertiary Symptoms developed.	1 year.	2 years.	3 years.	4 years.	5 years.	6 years.	7 years.	8 years.	9 years.	10 years.	11 years.	12 years.	13 years.	14 years.	15 years.	16 years.	17 years.	18 years.	19 years.	20 years.	20–25 years.	25–30 years.	Over 30 years.
101 Males	12 11·88 °/₀	10 9·9 °/₀	16 15·84 °/₀	5 4·95 °/₀	1 0·99 °/₀	7 6·93 °/₀	6 5·94 °/₀	6 5·94 °/₀	5 4·95 °/₀	3 2·97 °/₀	—	5 1·95 °/₀	1 0·99 °/₀	5 4·95 °/₀	—	1 0·99 °/₀	1 0·99 °/₀	1 0·99 °/₀	3 2·97 °/₀	6 5·94 °/₀	3 2·97 °/₀	2 1·98 °/₀	2 1·98 °/₀
73 Females ...	2 2·72 °/₀	11 15·07 °/₀	2 2·72 °/₀	5 6·84 °/₀	3 4·1 °/₀	6 8·21 °/₀	8 10·95 °/₀	5 6·84 °/₀	5 6·84 °/₀	1 1·37 °/₀	2 2·72 °/₀	3 4·1 °/₀	1 1·37 °/₀	3 4·1 °/₀	6 8·2 °/₀	2 2·72 °/₀	2 2·72 °/₀	1 1·37 °/₀	—	—	1 1·37 °/₀	3 4·1 °/₀	1 1·37 °/₀

Primary Lesions.	Quite Overlooked	Phagedænic.	Extra-genital.	Secondary Manifestations.	Quite Overlooked.	One Attack.	Two Attacks.	Three Attacks.	More Attacks.	Nature of Secondary Manifestations.	Macular Exanthem.	Papular Exanthem.	Of Mucous Membrane.	Condylomata.
Males	38 26·2 °/₀	2 1·4 °/₀	—	Males	54 37·2 °/₀	27 18·6 °/₀	9 6·1 °/₀	1 0·69 °/₀	2 1·38 °/₀	Males	18	6	18	4
Females	100 57·47 °/₀	—	2 1·14 °/₀	Females	105 60·3 °/₀	26 14·9 °/₀	7 4·02 °/₀	1 0·57 °/₀	2 1·14 °/₀	Females	10	10	17	23

Treatment in Secondary Period.	Absolutely Untreated with Mercury.	Only Treated Locally.	Certainly badly Treated.	Inadequately Treated.				Totals.	Chronic Intermittent Treatment.	Several Mercurial Courses only commenced a considerable time after Infection.
				One Course.	Two Courses.	Three Courses.	Several Courses.			
Males	71 48·9 °/₀	6 4·1 °/₀	28 19·3 °/₀	30	4	1	—	35 23·45 °/₀	3 2·07 °/₀	2 1·3 °/₀
Females	124 71·25 °/₀	4 2·29 °/₀	12 6·89 °/₀	25	3	1	—	29 16·65 °/₀	—	5 2·85 °/₀

Nature of Tertiary Lesions.	Skin.	Mucous Membrane.	Bone, Cartilage, Periosteum.	Nervous System.		Internal Organs.	Tongue.	Testicle.	Muscle.	Eye.	How often attacked with Tertiary Lesions.	Once.	Twice.	Thrice or oftener.
				Brain.	Spinal Cord.									
Males	101 69·6 °/₀	30 20·6 °/₀	45 31·0 °/₀	12 8·2 °/₀	1 0·7 °/₀	2 1·3 °/₀	5 3·4 °/₀	10 6·8 °/₀	1 0·7 °/₀	1 0·7 °/₀	133 Males	87 65·4 °/₀	28 21 °/₀	18 13·6 °/₀
Females	111 63·8 °/₀	66 37·9 °/₀	53 30·5 °/₀	8 4·6 °/₀	—	1 0·57 °/₀	1 0·57 °/₀	—	2 1·1 °/₀	1 0·57 °/₀	151 Females	91 60·26 °/₀	36 23·84 °/₀	24 15·96 °/₀

Multiplicity of Tertiary Lesions.	Period after Infection.					
	1 year.	2 years.	3 years.	4 years.	Later.	Date of Infection Unknown.
Males	7	1	2	1	5	4
Females	1	4	—	—	7	9

* As mentioned, these figures relate to cases in which I could find definite statements in the notes regarding the treatment in the Secondary Period. Where figures differing from this number are met with in other connections, this is due to my having, in all instances, only included those cases in which the notes afforded positive or negative statements regarding the particular points under discussion.

TABLE II.—PRIVATE MATERIAL.

244 cases of Professor Neisser's, including 218 Males (89·4 °/₀) and 26 Females (10·6 °/₀), and 110 cases of my own, comprising 99 Males (90 °/₀) and 11 Females (10 °/₀).*

Age.	1—10.	10—20.	20—30.	30—40.	40—50.	50—60.	60—70.	Over 70.
66 Males	—	1 1·5 °/₀	20 30·30 °/₀	28 42·42 °/₀	12 17·87 °/₀	3 4·54 °/₀	2 3·03 °/₀	—
13 Females	1	1	1	6	2	2	—	—
93 Males	—	—	25 26·88 °/₀	37 39·78 °/₀	23 24·73 °/₀	7 7·52 °/₀	1 1·07 °/₀	—
10 Females	—	—	3	5	1	1	—	—

Period of Development of Tertiary Symptoms after Infection.	1 year.	2 years.	3 years.	4 years.	5 years.	6 years.	7 years.	8 years.	9 years.	10 years.	11 years.	12 years.	13 years.	14 years.	15 years	16 years.	17 years.	18 years.	19 years.	20 years.	20–25 years	25–30 years.	More than 30 years.
193 Males	11 5·7 °/₀	21 10·8 °/₀	24 12·4 °/₀	20 10·4 °/₀	22 11·9 °/₀	16 8·3 °/₀	4 2·1 °/₀	15 7·7 °/₀	9 4·6 °/₀	8 4·2 °/₀	8 4·2 °/₀	3 1·5 °/₀	2 1 °/₀	4 2·1 °/₀	5 2·6 °/₀	3 1·5 °/₀	3 1·5 °/₀	4 2·1 °/₀	2 1 °/₀	2 1 °/₀	6 3·1 °/₀	1 0·5 °/₀	—
12 Females ...	2 16·6 °/₀	1 8·33 °/₀	—	—	—	1 8·33 °/₀	1 8·33 °/₀	3 25·0 °/₀	1 8·33 °/₀	1 8·33 °/₀	—	1 8·33 °/₀	—	—	—	—	—	—	—	—	1 8·33 °/₀	—	—
92 Males	4 4·3 °/₀	11 11·9 °/₀	14 15·2 °/₀	10 10·8 °/₀	9 9·8 °/₀	9 9·8 °/₀	3 3·2 °/₀	2 2·2 °/₀	2 2·2 °/₀	2 2·2 °/₀	3 3·2 °/₀	2 2·2 °/₀	3 3·2 °/₀	1 1·1 °/₀	5 5·4 °/₀	2 2·2 °/₀	4 4·3 °/₀	1 1·1 °/₀	2 2·2 °/₀	—	2 2·2 °/₀	—	1
9 Females ...	1 11·1 °/₀	—	2 22·2 °/₀	1 11·1 °/₀	2 22·2 °/₀	—	2 22·2 °/₀	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—

Primary Lesions.	Entirely Overlooked	Phagedænic.	Extra-genital.	Secondary Manifestations.	Entirely Overlooked.	One Attack.	Two Attacks.	Three Attacks.	More Attacks.	Nature of Secondary Manifestations.	Macular Exanthem.	Papular Exanthem.	Of Mucous Membrane.	Condylomata.
Males	14 6·4 °/₀	—	—	Males	38 17·4 °/₀	13 5·9 °/₀	17 7·8 °/₀	4 1·8 °/₀	17 7·8 °/₀	Males	34 15·6 °/₀	6 2·7 °/₀	39 17·9 °/₀	12 5·5 °/₀
Females	11 42·3 °/₀	—	—	Females	11 42·3 °/₀	—	1	—	—	Females	—	2	2	1
Males	4 4·04 °/₀	3 3·03 °/₀	—	Males	10 10·1 °/₀	21 21·2 °/₀	5 5·05 °/₀	1 1·01 °/₀	3 3·03 °/₀	Males	14 14·1 °/₀	1 1·01 °/₀	7 7·07 °/₀	—
Females	3 27·2 °/₀	—	—	Female	3 27·2 °/₀	1	—	—	—	Females	—	—	—	—

Treatment during Secondary Period.	Absolutely Untreated with Mercury.	Only Treated Locally.	Certainly badly Treated.	Inadequately Treated.				Totals.	Chronic Intermittent Treatment.	Several Mercurial Courses only commenced a considerable time after Infection.
				One Course.	Two Courses.	Three Courses.	Several Courses.			
Males	52 28·8 °/₀	3 1·7 °/₀	46 21 °/₀	52	32	12	7	103 47·3 °/₀	6 2·6 °/₀	8 3·6 °/₀
Females	15 57·7 °/₀	—	5 19·2 °/₀	3	1	1	1	6 23·1 °/₀	—	—
Males	23 23·17 °/₀	—	30 30·3 °/₀	35	7	3	1	46 46·41 °/₀	—	—
Females	5 45·4 °/₀	—	1 9·09 °/₀	3	1	—	1	5 45·39 °/₀	—	—

Nature of Tertiary Lesions.	Skin.	Mucous Membrane.	Bone, Cartilage, Periosteum.	Nervous System.		Internal Organs.	Tongue.	Testicle.	Muscle.	Eye.	How often attacked with Tertiary Lesions.	Once.	Twice.	Thrice or oftener.
				Brain.	Spinal Cord.									
Males	118 54·1 °/₀	28 12·8 °/₀	34 15·6 °/₀	33 15·1 °/₀	6 2·7 °/₀	1 0·6 °/₀	9 4·1 °/₀	14 6·4 °/₀	1 0·6 °/₀	7 3·2 °/₀	213 Males	154 70·6 °/₀	47 21·5 °/₀	12 5·5 °/₀
Females	14 53·8 °/₀	5 19·2 °/₀	6 23 °/₀	2 7·7 °/₀	—	—	1 3·8 °/₀	—	1 3·8 °/₀	1 3·8 °/₀	25 Females	21 80·7 °/₀	4 19·3 °/₀	—
Males	37 37·3 °/₀	14 14·1 °/₀	31 31·3 °/₀	18 18·1 °/₀	4 4·04 °/₀	1 1·01 °/₀	12 12·1 °/₀	4 4·04 °/₀	—	8 8·08 °/₀	99 Males	74 74·7 °/₀	22 22·2 °/₀	3 3·03 °/₀
Females	3 27·2 °/₀	1 9·09 °/₀	4 36·3 °/₀	3 27·2 °/₀	—	—	1 9·09 °/₀	—	—	1 9·09 °/₀	11 Females	8 72·7 °/₀	3 27·3 °/₀	—

* I have arranged the statistics of the two sets of cases separately in order to facilitate their inspection and comparison. The upper sets of cases are Professor Neisser's, the lower my own.

of tertiary syphilis among women than among men; and in contrast to these stand the percentages in the private statistics with a mean percentage of 89·7 per cent. of males to 10·3 per cent. of females affected. In this connection the figures of both sets of private statistics are in almost complete accord. Undoubtedly the apparent difference between the hospital and private statistics is due to the fact that syphilis is very far rarer among women of the better class than by those met with in hospital practice. Perhaps the further fact also comes in that among the latter it is much more liable to be overlooked in its early stages than among the former.

II. As regards ages, our statistics are in almost complete agreement with those of others in showing that tertiary syphilis most frequently develops at middle ages, between 20 and 40; and I found, by reckoning male and female hospital cases together—

Between 20-30 years	... ...	29·6 per cent.
,, 30-40 ,, ...	... ...	34·9 ,,
,, 40-50 ,, ...	... ...	18·9 ,,

We see, further, that the numbers rapidly fall off between the 40th and 60th years, and after the 70th year the disease hardly occurs at all. Equally small is the number of cases between the 10th and 20th years, 4·5 per cent., and between the 1st and 10th year they only reach 0·6 per cent.

Exactly the same is found among the private cases, as may be seen from the tables.

III. A more important question is the period after infection of the occurrence of tertiary affections.

The results of our statistics, collected from private practice, agree almost exactly with those of Fournier, also derived from private practice. The number of tertiary affections increased up to the third year, and even in the first year, is considerable; reaches a maximum in the third year and then gradually decreases, the numbers in the fourth year being about equal to those of the second. After the tenth year the falling off is no longer so striking; between the twenty-fifth and thirtieth years after infection only isolated cases are met with, and after the thirtieth year they are extremely rare.

Among the hospital cases the maximum of tertiary affections falls in the second year after infection. The reason for this is,

as we shall presently see, that among such patients the mercurial treatment in the early period is usually much less thorough and adequate than among private patients; and a far larger number of patients have received no treatment at all.

Even here, however, most are attacked in the second, third, and fourth years, just as in Fournier's statistics. After the thirtieth year, 16 per cent. of the cases still occur.

At this point I must anticipate an objection which may be raised by anyone who has not himself drawn up statistics of the frequency of tertiary eruptions according to the duration of the disease, and who forms an opinion based upon his "recollection," viz., have there not been included among "tertiary" cases occurring in the earliest years a number of ill-diagnosed or ill-characterised affections, such as ulcerated papules, crusted lesions, and the like?

I have rejected all notes (relating to the early years) which contain nothing more complete than the diagnosis ulcus lueticum and the like, and the number of tertiary cases in the three first years appeared to us so remarkably large, that I sought to avoid self-deception by the exercise of special care. I must make a special reference to the peculiar conclusions which Lang draws from Fournier's statistical tables bearing upon the period of development of tertiary symptoms.

Without himself adopting the statistical method, he questions from his own material the frequency assigned by Fournier to tertiary syphilis in the first three years (which all later workers have confirmed), a course which I must regard as inadmissible from my own experience. Both Professor Neisser and I were very much astonished that in our statistics also so many tertiary eruptions were to be assigned to the first years of syphilis, for we, like Lang, had expected from our recollection a much smaller percentage. We must then await Lang's own statistics.

To us, Lang's conclusion "that the growth of the tertiary cases in the first years to so high a total must be due to the periodic treatment of Fournier." Does Lang overlook the fact that Fournier's cases, like our own, were in the great majority of instances untreated, or only treated, according to Lang's own principles, in as far as was required by the symptoms? How then can there be any question of an unfavourable influence of

Fournier's periodic treatment? Is it not much rather to be ascribed to Lang's own views?

IV. As regards the primary affection, we find that among the hospital cases in 26·2 per cent. of the males, and 57·4 per cent. of the females, no primary lesion was observed; but seeing that these figures only related to cases in which I found statements on this point in the notes, we must assume that these percentages are still too small.

Phagedænic primary lesions I found in only 1·4 per cent. of males, extra-genital primary lesion only in 1·1 per cent. of females.

The same holds good for secondary symptoms, which were not observed at all in 37·2 per cent. of the males and in 60·3 per cent. of the females. These figures also are probably too small, seeing that in only 234 cases out of 319 were definite (positive or negative) statements found. They were observed once only in 18·6 per cent. of the males and 14·9 per cent. of the females, and they occurred more than thrice in only 1·3 per cent. of males and 1·1 per cent. of females.

Nor were the types of the secondary manifestations at all characteristic, and it cannot be by any means stated that the more severe forms predominated. In the small number of cases I found definite data on this point in the notes. Roseola occurred in 18 of the male cases, papular exanthemata in 6, mucous tubercles in 18 cases, and condylomata in 4. Among the females, on the other hand, there was roseola in 10 cases, papular exanthemata in 10, mucous tubercles in 17, and papules on the genitalia in 23 cases.

An examination of the private cases yields the following data: Absolutely no primary affection was noticed in 6·4 per cent. (N.)* and 4·0 per cent. (M.) of the males, and in 42·3 per cent. (N.) and 27·2 per cent. (M.) of the females. Phagedænic primary lesions occurred in only 3·0 per cent. (M.) of the males.

No secondary symptoms at all were observed in 17·4 per cent. (N.) and 10·1 per cent. (M.) of the male cases, and 42·3 per cent. (N.) and 27·2 per cent. (M.) of the females. Moreover, in 13·5 per cent. (on an average) secondary symptoms were only once

* The "N." and "M" after the several figures indicate, as guides, the cases of Professor Neisser and my own cases respectively.

observed, and we met with such symptoms on more than three occasions in 5·4 per cent.

Roseola occurred most frequently in 34 cases out of 91 (N.) among males, and 14 male cases out of 22 (M.). Then came mucous tubercles with 39 (N.) and 7 (M.) cases respectively.

On comparing as regards this point the hospital with the private material we find that the results are in the main identical. The fact that among the hospital cases the numbers of those who had not observed any primary or secondary manifestations is, of course, due to the fact that the more intelligent patients less frequently overlook an infection. This difference is, however, only striking among the men, whereas among women the number of those who noticed neither primary nor secondary manifestations is always greater than among men. In the hospital statistics 57·4 per cent., 26·2 per cent. as regards the primary lesion, and 60·3 per cent., 37·2 per cent. as regards secondary manifestations. In the private cases the relation is 6·4 per cent. (N.) and 4·0 per cent. (M.) males, to 42·3 per cent. (N.) and 27·2 per cent. (M.) females who observed no primary lesion at all, and 17·4 per cent. (N.) and 10·1 per cent. (M.) males, as against 42·3 per cent. (N.) and 27·2 per cent. (M.) females who overlooked their secondary manifestations.

It follows from this that women overlook primary and secondary manifestations much more readily than men, so much so that differences in self-observation among patients in private and in hospital practice respectively is conspicuously shown amongst the men by the figures quoted, but not amongst the women. Phagedænic ulcers occurred in only a very minute number of cases, and this shows that the quality of the primary lesion has no influence at all upon the development of tertiary symptoms.

As regards secondary manifestations, we see that the majority of patients have only observed these on one occasion; whereas the number of those who have been repeatedly attacked is less. Moreover, when we take into consideration the form of the secondary lesions, we see that in most cases quite slight symptoms, such as roseola and mucous tubercles, showed themselves, and papular exanthemata were much rarer.

It would seem, then, that the nature and frequency of the secondary symptoms have no influence upon the occurrence of tertiary ones, and that we have not been able to find any basis

for the views of those authors who maintain that the occurrence of tertiary can be foretold from the secondary manifestations, and that after severe primary and secondary lesions one must be prepared for tertiary symptoms.

We rather lean to the contrary view, that in the great majority of instances tertiary manifestations develop after quite slight primary and secondary stages, owing to the fact that on the older principles of treatment of syphilis, against which we have been contending, such slight cases have been, as a rule, not treated at all or quite insufficiently treated.

V. The most important point in our labours relates to the establishing of the treatment carried out in the secondary stage.

In this connection I have adopted in the statistics the following classification:—

1. Cases absolutely untreated.

2. Those only treated locally—two classes which are from our point of view practically the same.

3. Cases certainly badly treated—that is to say, those who have only undergone a too short mercurial course, or one not methodically carried out. On this point far too little stress has been laid, in my opinion, in ascertaining the histories. In innumerable instances it can be shown by adequate inquiry that "courses" mentioned by the patients as a matter of fact cannot and should not be reckoned.

4. Insufficiently treated cases, in which one or more methodically conducted courses have been undergone. Here I have made four subdivisions according as one, two, three, or more courses have been undergone.

5. Cases treated on the chronic intermittent plan, that is to say, from the commencement of the disease for two years at least. I have already explained that when possible we extend this treatment even over the third and fourth years, but I have included cases treated for two years in this class, with some detriment to my statistical results.

6. Cases in which repeated energetic mercurial courses were carried out, but only commencing at a late period, that is to say, some months after the onset of the secondary manifestations, and sometimes even later; these patients remained with recent syphilitic manifestations upon them for some months without mercurial treatment.

If we consider first the hospital in and out-patients, we find the following data :—

1. 53 per cent. of the males and 73·5 per cent. of the females had undergone no general mercurial treatment (those who had been only locally treated being here included).

2. 19·3 per cent. of the males and 6·8 per cent. of the females had been badly treated.

3. 23·9 per cent. of the males and 16·6 per cent. of the females had been inadequately treated. Most of the cases in this class had only undergone a single systematic course. Among 35 men, 30 had had a single course, 4 two courses, and 1 only three courses; none had had a larger number. Among 29 women in this class, there had been a single course in 25 cases, two courses in 3, and three courses in 1 instance. Here also no larger number of courses had been undergone.

4. Only 3 males out of 145 had been treated on the chronic intermittent plan, that is, a percentage of 2·07; among the women there were no cases so treated, and if we reckon these 3 out of a total of 319 hospital patients, we obtain a percentage of 0·9, that is to say, not quite 1 per cent. of the hospital patients suffering from tertiary syphilis had undergone in the early stages a liberal intermittent mercurial treatment extending over at least two years.

5. Repeated courses of mercury, but only commenced some time after infection, had been undergone, by 2 males (1·3 per cent.) and by 5 females (2·8 per cent.).

These figures undoubtedly show differences between treated and untreated cases which are certainly very striking. Here I may repeat that I have only included in the statistics those cases in which I found in the notes definite, positive, or negative data, regarding the past treatment, whereas cases (of which there were many) in which it was more than probable that there had been practically no treatment, but in which no definite statement to that effect was contained in the notes, have not been included. Had I included such, the difference between the treated and untreated cases would have appeared much greater.

The enormous number of cases included in the class "practically untreated or only quite inadequately treated," is easily understood if we consider that we are dealing with hospital in and out-patients.

Among the private cases we still see very clearly the great ætiological importance of mercurial treatment as regards the occurrence of tertiary manifestations, but yet in different proportions than among the hospital cases.

These cases yield the following data :—

1. Among the males 55 (N.) = 25·1 per cent., and 23 (M.) = 23·1 per cent. (mean = 24·1 per cent.) had undergone no treatment at all, which is less than half the proportion among the hospital cases. Among the female private patients we find the same relation as was noticed above in connection with the history of the primary and secondary manifestations, namely, that even in the better classes there were far more women than men who were absolutely untreated, the figures being 57·7 per cent. (N.) and 45·4 per cent. (M.), mean = 51·6 per cent., a percentage which is certainly lower than the 73·5 per cent. of absolutely untreated women in the hospital material, but which must nevertheless be regarded as very high when compared with the 24·1 per cent. of male private patients.

2. Of the males 21 per cent. (N.) and 30·3 per cent. (M.), mean = 25·6 per cent., and of the females 19·2 per cent. (N.) and 9·0 per cent. (M.), mean = 14·1 per cent., had certainly been badly treated.

3. 47·3 per cent. (N.) and 46·4 per cent. (M.) of the male patients, mean = 46·8 per cent., and 23·1 per cent. (N.) and 45·3 per cent. (M.) of the women, mean = 34·2 per cent., had been insufficiently treated.

As regards the number of courses undergone by the individual patients we here find a much larger proportion of cases who had undergone two to three, or even more courses than was the case among hospital patients, but nevertheless those with a single course still greatly preponderate.

The numbers of courses were distributed as follows :—

		1 course.	2 courses.	3 courses.	More than 3 courses.
Males	N.	52	32	12	7
	M.	35	7	3	1
Females	N.	3	1	1	1
	M.	3	1	—	1

4. The chronic intermittent mercurial treatment had been applied in only 6 cases (all 6 patients being Prof. Neisser's), which, when brought into relation with his total of 244 cases

which are included in the statistics, yield a percentage of 2·6. If, however, we include all the 354 cases contained in both sets of statistics we obtain the figure of only 1·69 per cent. Among my patients which I have seen in my practice at a bath place I have not met with a single one who had undergone a chronic intermittent mercurial treatment, because in the countries from which my patients mostly come such treatment is as yet not employed at all, or only to a very limited extent.

So, then, even among the private patients who had been in general comparatively far better treated, and who had, as is seen from the statistics, undergone many more mercurial courses, one finds not quite two in a hundred who had undergone chronic intermittent treatment and had developed tertiary symptoms.

5. In eight cases were developed tertiary syphilis in spite of several mercurial courses. They had not been subjected to the chronic intermittent treatment, but had nevertheless undergone three ordinary mercurial courses on an average.

I think, as I have already repeatedly set forth, that these cases should be separately dealt with, because in spite of recent and obvious syphilis they had remained for a long time without treatment.

Among the hospital patients also there were seven cases of this character.

If I attempt to draw general conclusions from all our figures, the following facts are established* :—

1. Among the patients with tertiary syphilis the totals of 1·3 per cent. of well (chronic intermittently) treated cases, and of 98·7 per cent. of badly treated or quite untreated cases, stand in contrast with each other.

2. If I place on the one side the total of all those who have undergone at least three courses (*i.e.*, moderately well treated), and on the other side all patients with one or two courses, and the untreated cases, the relation is as follows :—

In Neisser's private practice—			
Males, with three or more courses,	11·4 per cent.	With less than three courses,	88·6 per cent.
Females ,, ,,	7·7 ,,	,, ,,	92·3 ,,

* The basis for these and the following figures is afforded by a table, in which (not as in the principal tables) the figures are grouped in yet another manner, with special reference to the number of individual courses, and which I here reproduce.

In Merschalko's private practice—
Males, with three or more courses, 4·0 per cent. With less than three courses, 96 per cent.
Females „ „ 9·0 „ „ „ 91 „
In hospital practice—
Males, with three or more courses, 2·6 per cent. With less than three courses, 97·4 per cent.
Females „ „ 0·57 „ „ „ 99·43 „

HOSPITAL MATERIAL.

Treatment in Secondary Period.	Absolutely Untreated.	Only Treated Locally.	Badly Treated.	Moderately Treated (3 courses).	Intermitting Mercurial Treatment for at least 2 years.	Numerous Mercurial Courses only long after Infection.
Males	71 48·9 %	6 4·1 %	62 42·6 %	1 0·65 %	3 1·95 %	2 1·3 %
Females	124 71·25 %	4 2·29 %	40 22·97 %	1 0·57 %	—	5 2·85 %

PRIVATE MATERIAL.

Males	52 23·8 %	3 1·3 %	130 59·6 %	19 8·7 %	6 2·6 %	8 3·6 %
Females	15 57·7 %	—	9 34·6 %	2 7·7 %	—	—
Males	23 23·17 %	—	72 72·7 %	4 4·0 %	—	—
Females	5 45·4 %	—	5 45·4 %	1 9·0 %	—	—

3. If we take, on the one hand, the untreated cases and those who have not undergone a single systematic mercurial course, and on the other hand all those treated (even including those who have only undergone a single thorough course) we obtain the following figures:—

In Neisser's private practice—
Males untreated 46·3 per cent.; thoroughly treated at least once 53·7 per cent.
Females „ 76·1 „ „ „ „ 23·9 „
In Marschalko's private practice—
Males untreated 53·5 per cent.; thoroughly treated at least once 46·5 per cent.
Females „ 54·5 „ „ „ „ 45·5 „
In hospital practice—
Males untreated 71·0 per cent.; thoroughly treated at least once 29 per cent.
Females „ 80·5 „ „ „ „ 19·5 „

Which table ought we to take as the basis of our conclusions?

The first, with its so strikingly favourable indications of the value of the chronic intermittent treatment, is specially open to the objections—

1. That the absolute numbers are too small to allow of general conclusions being drawn from them.

2. That the period of observation of cases so treated is too short, and that it is possible that a number of such patients may yet develop tertiary lesions.

However, even if we accept these objections as unquestionably justified in part, we must still admit that we ourselves were surprised at the smallness of these figures, seeing that on the one hand the chronic intermittent treatment has been carried out in Breslau on hundreds of patients during the past ten years, a large proportion of whom have remained under observation for long periods, and would have certainly have come under notice for any tertiary manifestations. Moreover, it appears from the statistics of tertiary syphilis that in the immense majority of cases the tertiary symptoms develop in the first few years after infection. The brevity of the period of observation cannot then have any such crucial importance, since at the worst one must conclude that the chronic treatment does not diminish the number of tertiary attacks, but only postpones the period of their occurrence, a view for which no positive evidence of any kind is forthcoming.

Again, the figures on which the second table is based are too small, especially for the hospital patients. The differences are striking between the private and hospital patients, and these are due to the fact that in the private material the number of patients who have undergone at least three courses is much larger than in the hospital material.

This difference is still greater in the third table, in which, among the hospital patients, the total of those not even once thoroughly treated with mercury is far larger in hospital than in private practice, and especially than among the male private patients. This difference is doubtless due to the fact that private patients with venereal affections at least visit a medical man at the onset, and are therefore better treated. In women early syphilis is easily overlooked even in private practice.

It is from these various groupings of my material that bring out very clearly the influence of treatment upon the develop-

ment of tertiary syphilis, and it is unnecessary for me to insist once again that I have been very conscious of the sources of error which underlie statistics of this kind.

The figures which I have been able to place together gain still further importance by comparison with the results of other authors which I reproduce in the following table :—

Fournier.		Husland.	Vajda.	Hjelmann.
1	2			
Among 100 cases of cerebral syphilis only 5 per cent. had been well (*Sérieux*) treated, and 95 per cent. inadeqnately, for a short time, for too short a time, or not at all.	Among 1,073 cases of tertiary syphilis, only in 59 cases had there been thorough treatment (during two years) *i.e.*, in 3·4 per cent., and among these only 6 had undergone a prolonged intermittent treatment extending over at least three years, = 0·35 per cent.	86·75 per cent. of all cases were not treated with mercury at all, or only very imperfectly treated. In the remainder the treatment apparently left nothing to be desired. It is not stated whether as a rule, or in how many cases, chronic intermittent treatment was carried out.	62 per cent. previously quite untreated, only 12·1 per cent. previously treated with mercury. (To what extent and how often is not stated.)	83 to 88 per cent. previously either absolutely untreated, or quite inadequately treated, with mercury.

From a comparison of this table with mine it is sufficiently evident that in such statistics it is quite necessary to group the cases in many classes as far as possible according to the kind (*i.e.*, the amount) of treatment undergone, and to deal with those actually treated by the chronic-intermittent method quite separately, as Fournier has actually done. As long as the number of cases so treated remains relatively small compared with the total of syphilitic patients, we must continue to consider the differences between the other groups as I have done above.

IV. As regards the quality of the tertiary symptoms and their incidence upon the several organs, in our statistics skin affections preponderate. Among the hospital patients we find such in 69·6 per cent. of the males, and in 63·8 per cent. of the

females, giving a mean of 66·7 per cent. Among the private patients the figure is not so high, although amongst these also skin affections were observed in males and females; in both sets of private statistics taken together is an average of 43·1 per cent. of all cases.

The figures doubtless do not give any absolute measure of the true frequency of the several tertiary localisations. Dermatological institutions and practitioners receive naturally an excessive supply of cutaneous syphilitic material.

How strikingly different such figures may work out as the result of quite accidental differences in the material is seen by a comparison of the two sets of private statistics. Whereas in Professor Neisser's private practice the percentage of skin affections reaches 53·9 per cent., they were present in my watering-place practice in only 32·2 of the tertiary cases, which is easily explained by the circumstance that in a bath place all persons with severe tertiary affections are collected together without any regard to their localisation.

The difference is still more striking if we compare the other classes included in the hospital statistics with both sets of private statistics, or if we compare these latter with each other.

Whereas, for example, affections of the osseous system (bone, cartilage, and periosteum) take in all the tables the second or third place in the scale of frequency, with almost identical percentages (30·7 as against 26·5 per cent.), diseases of the nervous system only attain to 6·5 per cent. in the hospital material, as against 18·9 per cent. in the private material.

When, again, we compare the figures of the two sets of private statistics with each other, we find the tertiary affections of the nervous system constituting among Professor Neisser's cases 16·7 per cent., amongst mine 22·7 per cent. (or almost a quarter of the entire number of tertiary syphilitic cases).

I have already expressed my opinion at length as to the inclusion of tabes and paralysis under tertiary syphilis. A more detailed discussion of the question of localisation appears to me to be superfluous, and I am unfortunately not able to discuss here the question of the connection between injury and tertiary localisations; I will reserve what I have to say upon this point for a future occasion.

In conclusion, I may be allowed to throw some further light upon three points by the aid of my statistics.

(1) The first relates to the question where there exists any relation between the multiplicity of tertiary symptoms, that is to say, the number of individual foci of disease which appear simultaneously, and the period of their development.

From the course of syphilis in general, and especially from our experience of cutaneous syphilides, one might infer that the fresher a tertiary affection is, *i.e.*, the earlier after infection it develops, so much the more readily and more frequently will the tertiary symptoms assume a multiple development. In this connection I have thoroughly gone over the cases in the hospital statistics, and have actually found that, especially among the males, the cases exhibiting such multiplicity, even in the earliest years after infection, are strikingly numerous.

Among 20 cases with multiple manifestations of tertiary syphilis which I was able to examine, multiple tertiary symptoms had already developed during the first year after infection in 7, in 1 during the second year, in 3 during the third year, in 1 during the fourth year, and in 5 at a later period.

Moreover, in 4 cases the date of infection was uncertain, so that if we exclude these cases, multiple tertiary manifestations occurred as early as during the first year after infection in almost 50 per cent. of the cases. The number of these cases is naturally much too scanty to allow of final conclusions being drawn from them, but nevertheless they appear to support the view, which moreover, as has been pointed out, is in accord with the whole nature of the disease, that the numbers in which multiple tertiary symptoms occur is inversely proportional to the duration of the disease as a whole.

(2) The second point relates to the question whether as regards the period of development of tertiary lesions after the infection there is any difference between the cases treated with mercury and those not so treated. Fournier has already touched upon this question, and in his text-book "Traitement de la Syphilis" has constructed two small tables bearing upon it. He arrived at the following results:—

Among 12 patients who in the early period were treated at least once with mercury, and who afterwards developed tertiary lesions, the minimum interval between infection and

the occurrence of tertiary symptoms was nine years, the maximum thirty-four years; on the other hand he observed 63 patients with tertiary syphilis who previously had been absolutely untreated with mercury, and found that of these, 53 developed tertiary symptoms as early as during the first ten years, and that the maximum of attacks fell between the second and fourth years (24 cases).

Vajda[69] also showed, as I have already mentioned, that those who were previously untreated developed tertiary symptoms after three years and seven months, on an average, whereas those who had been previously treated only showed tertiary manifestations after a much longer time, after seven years and four months, on an average.

I have carefully gone over the material of my statistics from this point of view, and have constructed the following table from 155 cases in which I found certain data, and which are taken in part from the hospital and in part from the private material.

Number of years after infection.	Absolutely untreated with mercury.	Certainly badly treated.	Insufficiently treated.	Well treated.
1	7	2	6	2
2	6	7	3	3
3	5	4	8	—
4	3	—	5	1
5	1	—	2	—
6	5	1	5	1
7	1	1	8	1
8	3	1	5	—
9	2	—	3	—
10	2	—	5	—
11	1	1	2	—
12	3	—	3	—
13	1	—	1	—
14	4	1	3	—
15	3	1	1	—
16	—	1	—	—
17	—	—	—	1
18	3	—	1	—
19	—	2	—	—
20	2	2	—	—
20 to 25	4	1	1	—
25 to 30	2	—	1	—

We see then that I also arrived at practically the same result, since it is evident from this table that the cases absolutely untreated with mercury show the greatest number of attacks in the first three years, and the actual maximum, indeed, as early

as the first year after infection; it is about the same with the patients undoubtedly badly treated, who also had hardly been treated with mercury, except that here the maximum falls in the second year. Among the insufficiently treated cases who had undergone one or two mercurial courses, the number of attacks is more evenly distributed over the first ten years. It is certainly remarkable that among the 9 well-treated cases, the majority were also attacked in the two first years, and 2 as early as during the first year; but apart from the fact that the number of cases of this class generally is too small, we have here to deal in three instances (especially in both those of the first year and in one of those in the second) with cases of syphilis which at the commencement was quite benign, but in which, in spite of treatment, tertiary symptoms developed at the earliest possible moment, in one case as early as the eighth month after infection; that is to say, with cases which, even if we are not justified in including them in the category of malignant syphilis, exhibit a "sport" or abnormality, of course the cause of which we are not in a position to decipher.

We may assert then that in the great majority of instances in which tertiary syphilis develops in the earliest years, and especially in the first year after infection, we are dealing either with cases absolutely untreated with mercury or certainly badly treated. In those cases in which, despite energetic treatment, and often even during such treatment, in the course of an initially normal attack of syphilis, tertiary symptoms develop at the earliest possible period, we have, in my opinion, to do as a rule (assuming that the treatment was not commenced too late) with an abnormality, and it is highly probable that such patients would, if untreated, have been attacked even sooner and probably in a more severe manner by tertiary lesions.

The third point which I desire to raise is also one of great importance, although attention has not hitherto been paid to it in the statistics, namely, the question whether mercury exercises a preventive influence even in the tertiary stage; and whether mercurial treatment has more than any other form of medication the power of hindering relapses of tertiary affections?

Being convinced of the preventive action of mercury and of its effect upon the actual virus, we employ mercury in the treat-

ment of tertiary syphilis also in conjunction with iodide, the value of which we in no way under-estimate. In the clinic of Professor Neisser this plan of treatment has been in use for many years; and the results which I have obtained from the statistics appear to justify this method. I investigated the manner in which those cases in which tertiary syphilis developed twice or more often had been treated since the first appearance of the tertiary symptoms; whether they had taken iodide alone or mercury also, or whether they had been submitted to no specific medication. In 53 cases in which I found certain data in the notes, I arrived at the following results: only 10 had been treated with mercury on the first appearance of tertiary symptoms, 21 with iodide, and 22 were untreated.

We see then that of those cases treated with iodide alone, almost as many relapsed as of those not treated at all, whereas the number of those who, in spite of mercurial treatment, had repeated tertiary attacks, is less than half the number of those treated with iodide. This difference is too striking to be regarded as fortuitous. Here, too, the fact must be taken into consideration that the notes as a rule merely contained the entry "mercurial course," which very probably in most instances signifies a single course only, and it is doubtful whether even this was sufficiently energetic. We may suppose that if the mercurial treatment had been energetic or intermittent the number of relapses of tertiary manifestations would have been considerably less still.

In connection with my statistics I will still consider a point upon which they give no information, namely, the frequency of tertiary syphilis in general in relation to the total number of cases of syphilis.

The data bearing upon this point are taken from the statistics in the "Klinische Jahrbücher."

The total number of cases of tertiary syphilis at the Clinic and Policlinic for Skin Diseases in Bonn, from 1887-88 to 1890-91, amounted on an average to 7·1 per cent. of all syphilitic patients; at the Royal Clinic and Policlinic for Skin Diseases in Breslau, similarly reckoned, to 11·9 per cent.; at the Royal Clinic for Syphilis in Berlin, between 1888-89 and 1890-91, the average was only 3·3 per cent.

If, now, we take the mean of these three figures, the per-

centage of tertiary syphilis for Germany works out at 7·4 per cent. As a matter of fact, amongst a total of 4,782 syphilitic males there were 425 cases of tertiary syphilis (8·5 per cent.), whilst among 6,010 syphilitic females there were only 465 tertiary syphilitic cases, so that one may say generally that tertiary syphilis occurs more frequently in males than in females among hospital in- and out-patients also (that in the material from private practice it occurs incomparably more often in males than in females we saw from my statistics), but there are differences in the different cities. Thus in Breslau the percentage of tertiary syphilis among women was actually higher than among men (12·1 per cent. against 18·8 per cent.); in Bonn 4·5 per cent. among women and 8·2 per cent. among men; in Berlin 21·1 per cent. among women and 5 per cent. among men. At the medical policlinic in Göttingen only one case of tertiary syphilis occurred in the years 1888-89 and 1890-91 amongst 66 syphilitic cases, whereas at the surgical polyclinic at Königsberg from 1888-89 to 1889-90, amongst 252 cases of syphilis, there were 67 of tertiary syphilis, equal to 26·5 per cent., a further proof of the unequal distribution of tertiary syphilis at the various clinics.

The conclusions which are derived from my work may be embodied in the following propositions :—

1. Tertiary syphilis occurs (in Germany) in about 7·4 per cent. of all syphilitic cases; but this figure somewhat understates the true proportion, since it is obtained from the statistics of skin clinics, and a part of the tertiary syphilitic cases from the same material, which in the early stages sought cure in the skin department, distributes itself over other departments.

2. The majority of tertiary affections develop in the middle period of life, between the ages of twenty and forty-five years.

3. Tertiary manifestations appear most frequently a few years, one may say up to the sixth or eighth year, after infection. In my statistics the majority of affections occurred during the second and third years after affection, but they are nevertheless fairly frequent even in the first year. After the third year the numbers affected undergo a continuous diminution, for until the sixth year they still remain considerable. Between the twenty-fifth and thirtieth year they become very infrequent, and

after the thirtieth year after infection very few developments occur.

4. The quality of the primary and secondary affections and the frequency of relapses of the latter afford no indication regarding the further course, and do not allow of any conclusion being drawn as to the occurrence of tertiary lesions. These rather tend to develop in a large number of instances after overlooked or quite insignificant primary and especially secondary lesions.

5. The chief determining cause for the development of tertiary manifestations is the absolute absence or complete neglect, or, at least, inadequacy of mercurial treatment in the early stages. The chief protection against them is energetic and sufficiently long-continued mercurial treatment.

6. Among mercurial treatments the first place is taken by long-continued intermittent mercurial treatment. Patients treated on this plan are only attacked by tertiary lesions in a hardly appreciable number of cases.

7. It appears that mercurial treatment if too late commenced, even although ultimately energetic, is no longer capable of exercising so high a degree of restraint upon the occurrence of tertiary manifestations as treatment commenced immediately after infection or the eruption of secondary lesions. At any rate patients treated in the above manner are proportionately often attacked with tertiary syphilis. It seems, speaking generally, that the chief importance attaches to the first course, and this must therefore be carried out most conscientiously.

8. I was not able to extend my investigations to the parts played by other predisposing influences, mentioned by various authors, in the ætiology of tertiary syphilis, and my statistics afford no information on these points.

9. Tertiary cutaneous lesions are certainly the most frequent, since, although statistics as yet prepared are unable to afford any correct representation of the distribution of tertiary syphilis among the individual organs, such affections have occurred so numerously in our statistics (and in all others also, with the exception of Fournier's), that it may safely be assumed that they would continue to hold the first place, even if we should succeed in constructing a large mass of statistics, affording a better survey in this connection. Affections of the osseous system

occupy the second place. Diseases of the nervous system occur much more frequently among the patients of private than of hospital practice. Among the former they take the third place (affections of the mucous membranes standing fourth), whereas among the latter lesions of mucous membranes fall into the third place with a considerably higher number of cases.

10. Tertiary manifestations only occur once in more than two-thirds of the cases, more rarely twice, and still more rarely thrice, or yet more often.

11. Mercurial treatment exercises a preventive action even in the tertiary stage of syphilis; it alone is able to avert relapses of tertiary affection, whereas iodide is unable to do so. On this account a mixed mercurial and iodide medication is to be preferred in the treatment of tertiary syphilis.

FRESH STATISTICS OF 1,501 CASES

OF

TERTIARY SYPHILIS.

BY

DR. EHLERS,

of Copenhagen.

[From the Verhandlungen des IV. Deutschen Dermatologen Congresses.]

FRESH STATISTICS OF 1,501 CASES OF TERTIARY SYPHILIS.

By Dr. Ehlers.

In this nineteenth century certain syphilologists of the highest rank, such as Bärensprung, Hughes Bennett, and W. Boeck, have revived the old and erroneous theory of Falloppia that tertiary syphilitic manifestations are especially apt to develop in patients who have been treated, at an earlier stage, by mercurial inunctions; and although Kussmaul long ago disposed of these foolish notions of the anti-mercurialists, we still hear arguments for and against these notions from Armand Desprès in Paris, Hermann in Vienna, and Caesar Boeck in Christiana, who share these remarkable views.

On the other hand we have the modern doctrine that tertiary lesions are commonest in patients who have not been treated at all, or who have been insufficiently treated, with mercury.

Since the first Dermatological Congress, held in Paris in 1889, we have been in possession of several large sets of statistics by Fournier, Haslund, Vajda, Neumann, and Hjelmann, who are almost unanimously of opinion that tertiary symptoms occur most frequently in patients whose secondary manifestations have not been treated at all, or only insufficiently, with mercury.

These statistics have further taught us that tertiary affections occur with the greatest frequency during the first three or four years after the infection. The vast and classical statistics of Fournier have also fixed our attention upon the excessive frequency of the nervous manifestations of tertiary syphilis.

In Denmark, my revered teacher, Professor Haslund, has already collected statistics relating to 791 patients. These cases are derived from the period 1882—91, during which time Haslund was at the head of the department for skin diseases and syphilis in the Communal Hospital at Copenhagen.

I have now the honour, Gentlemen, to lay before you a similar set of statistics of 1,501 cases obtained from the same depart-

ment during the period 1864—81, that is to say during the eighteen years in which Dr. Engelsted was the director. The number of cases treated during the same period for the earlier developments of secondary syphilis was 6,816. That is to say, the relation of tertiary to secondary cases was as 1 : 4·54 = about 22 per cent. Vajda and Haslund, who give lower figures, reckoned the numbers in proportion to the total of cases of syphilis in general (relapsing as well as incipient cases), which mode of reckoning is less correct. At any rate the truth lies between 12·4 per cent. (Haslund's figure) and 22 per cent. (my own).

As regards the proportion of males to females my statistics show 817 males and 684 females = 54·4 per cent. men and 45·6 per cent. women; Haslund saw 57·4 per cent. men and 42·6 per cent. women. The relation of males to females with the earliest secondary eruptions was, during the same period, 56·6 per cent. men to 43·4 per cent. women. It would seem then that both in the tertiary and secondary stages there is a constant excess of males amounting to about 10 per cent. At least one cannot conclude as B. Vajda did, that women are more frequently affected with tertiary syphilis than men.

Braus (1873), Mauriac (1879), Fournier and Gandichier (1886) have completely upset the older notions of the chronology of tertiary syphilis. We now know that tertiary cases are commonest during the first three or four years after infection. My results, which are shown in my tables, agree very well with those of Fournier, except that my curves reach their maxima as early as in the second year. The male cases remain at about the same figure throughout the first four years, but on the other hand the female cases show a curve which reaches its culminating point as early as the second year, and from this point sinks rapidly until in the fifth year it has again fallen to the height of the first year. Where the curve passes the years 5, 10, 15, 20, and so on, small fluctuations or elevations are seen, due to temporary rises in the numbers of cases.

These deviations from the regular decline are easily explained by the tendency of the patients to reduce their statements to round numbers. For example, if a patient has been infected nine years previously he is likely to date the infection from 10 years ago.

After 20 years tertiary syphilis is very rare, but a few cases occurring after 40 years are included in my statistics, as in those of Fournier. However, a quarter of all the cases occur in the course of the first four years.

If we consider the chronology of the individual localisations separately, we see that iritides (30 cases) take the first place among the early tertiary manifestations. On the average they developed before the end of the second year.

Then follow the gummatous orchitides (23 cases) before the end of the fifth year.

Somewhat later comes the gummatous orchitides complicated by the simultaneous development of subcutaneous nodes (17 cases), and later still, in the seventh year, come the gummatous orchitides complicated by periostitis (15).

We are here speaking of average numbers of years only, which naturally exceed three or four, seeing that the period within which tertiary syphilitic processes in general develop extends over more than forty years.

In the fifth year also we meet with the isolated gummatous subcutaneous nodes (25).

In the sixth year we see the local grouped gummatous ulcerations (171), the arthritides (10), and the serpiginous ulcerations (82), and also the mixed bony and cutaneous lesions (98).

In the seventh year appear the ulcerative and destructive lesions of the nose, mouth, larynx, pharynx, &c. (278), and the cerebral affections, among which were hemiplegias (67), encephalopathies (21), and ocular paralyses (13).

In the seventh to eighth years the exostoses are added to the list, the exostoses on the tibia (49) occurring first in the seventh year; in the eighth year the exostoses of the cranium (35) and of other bones (47).

In the eighth year occur the lesions of the spinal cord, of which, however, but few cases are admitted to our department—myelitis (24 cases).

In the twelfth year fall 14 cases of ataxia.

If I were to devise for you a rough schema of the chronology of the several tertiary localisations, I should say—

In the second year occur the iritides.

In the fifth to eighth years the orchitides.

In the sixth year the cutaneous lesions predominate.

In the seventh year the cephalic lesions, including—

(*a*) External lesions, *i.e.*, ulcerative and destructive affections of the nose, mouth, larynx, pharynx, &c.

(*b*) Internal, *i.e.*, cerebral affections.

In the seventh to eighth years bone lesions predominate.

In the eighth to twelfth years spinal and meningeal affections are met with.

As to frequency, cutaneous lesions (*i.e.*, lesions of the skin and neighbouring tissues) occupy the first place in my statistics with 438 cases; next come the destructive nasal and pharyngeal lesions with 390 cases, bone lesions with 348 cases, and affections of the nervous system (302).

But as a matter of fact this last figure must be largely augmented, since our department does not as a rule receive syphilitic patients with grave nervous lesions. Ocular lesions too come under the care of the ophthalmic surgeons. Practically external lesions alone come under the observation of the syphilologist. If, for example, we desire to form an estimate of the numbers of patients with severe cerebro-spinal affections who are not included in our statistics, we find that in the department of our hospital devoted to nervous diseases there were under treatment during the period 1864—1881:—

	150	cases of	tabes.
	486	,,	general paralysis.
	172	,,	cerebral syphilis.
Total ...	808	,,	cerebro-spinal syphilis.

This number probably corresponds to the total of all syphilitic patients of the preceding years, one quarter of whom are almost constantly treated in our department for the first development of syphilis.

We can therefore, in all probability, appropriate a quarter of the above figure, viz., 202. The addition 202 + 302 = 504 gives a higher figure than for any other localisations, and is still too small.

The tertiary syphilitic manifestations affecting the nervous system are accordingly the most frequent of all, as Fournier has also stated.

It need cause no surprise that the nervous and cutaneous manifestations are the commonest of all, seeing that these lesions yield the most definite, subjective, and objective symptoms,

whereas we know almost nothing concerning the frequency with which syphilis becomes localised in the internal organs.

The future will fill in these gaps in our knowledge.

Lastly, we come to the great question of treatment, and we find that:—

1. In 107 cases (7·12 per cent.) it was not possible to ascertain the previous treatment.
2. In 655 cases (43·64 per cent.) the patient had never previously been treated with mercury.
3. In 606 cases only the primary attack was treated with mercury (40·38 per cent.).
4. In 133 cases (8·86 per cent.) two or more developments were treated with mercury.

Further investigations will show whether the conclusions which we draw from these figures are justified, but, in conclusion, I may add a few words regarding the practical consequences of our present views on the chronology of tertiary syphilis.

It has always been held that tertiary lesions are not infectious, but, on the other hand, we know that the capability of infection in syphilis may be retained for five, eight, or even ten years.

Tertiary manifestations are most common during the first four years after infection. What follows from this? That the dogma of the non-infectious character of tertiary syphilitic lesions calls for revision, at any rate as regards gummatous ulcers on the genitalia, which are in no respect different from chancres, and which occur very frequently.

As a small contribution to this revision, I will relate the following observation:—Three years ago I saw a married man who had married two years after infection (having only undergone a single mercurial course). His wife remained healthy and bore two healthy children. When the man came under my treatment eight years after infection and six after marriage, he had a gummatous ulcer on his penis, which quickly healed under mercury and iodide of potassium. However, two months later, his wife came under my care (having certainly been infected by her husband) with a papular syphilide all over her; and their third child was born syphilitic.

If gummatous ulcers of the penis be not infectious, I see no explanation of this case, for there was no question of a reinfection of the husband, who developed no secondary manifestations

(roseola), and who six months later came to me with gummatous orchitis.

	Previous treatment not known.		No previous mercurial treatment.		A single mercurial course.		Repeated courses of mercury.		Total.
	M.	F.	M.	F.	M.	F.	M.	F.	
Cutaneous ulcerations (various) ...	13	2	47	63	38	39	18	12	232
Serpiginous ulcerations	3	2	17	35	19	28	5	1	110
Cutaneous nodes	1	3	6	11	4	15	0	3	43
Nodular skin affections (various) ...	18	2	16	57	5	34	3	4	139
Ulcerative and destructive lesions of the noso, pharynx, and larynx ...	7	7	94	128	78	57	12	7	390
Exostoses on the tibia	3	4	14	9	19	13	2	4	68
Cranial nodes	1	1	10	8	19	4	1	1	45
Other nodes	2	1	13	12	23	11	4	1	67
Joint affections	...	1	1	3	3	4	...	2	14
Bone lesions and gummatous orchitides	5	...	6	...	2	...	2	...	15
Cutaneous lesions and gummatous orchitides	10	...	8	...	1	...	2	...	21
Gummatous orchitides	1	...	9	...	19	...	3	...	32
Malignant repeatedly relapsing lesions	...	...	4	2	10	3	4	...	23
Cerebral affections...	7	2	16	6	41	12	13	8	105
Ataxia	3	...	3	...	10	1	...	...	17
Myelitis	1	...	6	4	11	6	2	2	32
Hemiplegia	4	...	17	9	39	10	7	2	88
Ocular paralysis	1	...	2	4	8	2	1	1	19
Iritides	2	...	7	8	10	3	3	3	41
	82	25	296	359	357	249	82	51	
	107		655		606		133		1501

ON THE ETIOLOGY OF TABES

(LOCOMOTOR ATAXIA).

BY

WILHELM ERB,

Heidelberg.

TRANSLATED

BY

DR. R. W. FELKIN.

[NOTE.—An elaborated report of a lecture given at the Hospital for Nervous Diseases on December 9th, 1891.]

ON THE ETIOLOGY OF TABES (LOCOMOTOR ATAXIA).

By Wilhelm Erb.

Gentlemen,

In your future practice you will meet with no more frequent disease of the spinal cord than tabes. Among all the chronic spinal affections, it is by far the most frequent and important; lingering and insidious, it seizes its victim in the middle of the prime of life, as a rule never again to disappear. Constant invalidism, not infrequently accompanied by great suffering and disagreeable pains, is the lot of tabic patients, who, being crippled in their power of work, are a burden greatly to themselves, their families, and the community.

But however great the practical importance of this malady may be, it is far exceeded by the scientific interest which it presents and which is constantly renewed by the variety and difficulty of the subject. The wealth of symptoms presented in this disease is quite inexhaustible, and the anatomical changes which lie at the root of it are intricate and still insufficiently cleared up, while its primary cause and essential nature are obscure and much disputed. Indeed, the unprecedented number of scientific treatises on tabes, which have been published by thousands during the last twenty years, has brought us but slowly, step by step, forwards.

After having brought under your notice, Gentlemen, a series of patients suffering from tabes, in order to show you typical symptoms, with a small number of their variations, I would like to direct your attention to-day to the causes of this mysterious disease.

The scientific history of tabes does not date far back. The first definite description of it was given by Romberg (1) (1851), the next by Wunderlich (2) (1854); later Duchenne (3) (1857–61), with his well-known masterly touch, sketched afresh and

completed the delineation of its symptoms, and in the commencement of the sixties the grey degeneration of the posterior column was fixed upon as the anatomical seat of the malady by the researches of German and French investigators. It was, however, first in the seventies, when the tendon reflexes had been discovered and their almost constant absence in tabes proved, and when attention had been more and more directed to the appearances in the initial stage, that we reached an extraordinary certainty in the diagnosis of tabes and in its differentiation from all other chronic affections of the spinal cord.

With this then the true basis for the investigation of its causes was first reached.

If the statements of the older authors on this point are examined, the greatest uncertainty is met with; sometimes more or less gratuitous statements are made, but never based upon definite facts. Only two etiological causes are as a rule considered, viz., sexual excess and chill. Whereas Duchenne considers the etiology of tabes to be quite obscure and the influence of sexual excess to be doubtful, speaking chiefly of chill as the principal cause, Romberg (1851) holds that the seminal loss caused by excess and sexual irregularities is the most fruitful cause of tabes, but allows that chill, the "rheumatic process" and over-exertion are also factors. Leyden (4) (1863), however, rejects entirely sexual excess as a cause of tabes, and declares chill to be the most important and probably the only cause of the malady. When I add that Romberg and Wunderlich included bodily over-exertion as a cause; that Duchenne pointed out the frequent presence of syphilis in the previous history of tabic patients, without however laying great stress on the fact; that later (1872) he also mentions strong emotions; that Trousseau also acknowledged a nervous temperament to exercise a certain influence, and that Wunderlich brought forward concussion of the spine as a cause—everything is before us which until quite recently was to be known concerning the etiology of tabes. These views recur with unimportant modifications in the text-books of the seventies.

It was not until the end of the seventies that greater interest was aroused in the investigation of the etiology of this disease, when first in France A. Fournier (5) (1875), with whom agreed later Vulpian (1879), and Grasset (1879), and Gowers (6)

(1878-79), and then in Germany I myself (7) (1879-81) raised the question of the importance of syphilis in tabes. At first I was not at all convinced of this importance,* but very soon learnt better through my own investigations.

Numerous researches have been made since then, very many treatises have appeared on this question, and a discussion arose which at times was somewhat heated. Views which at first were entirely opposite have by degrees been reconciled, and gradually an almost complete accord on the fundamental facts has been reached.

Before however we proceed to discuss the results of research, the question may be permitted—what methods of research may be admissible and best employed in this enquiry?

In this case there is, as usual, only a question of two methods—experiment and clinical observation. The latter has either to establish the immediate onset of certain pernicious actions, or by means of statistics, to confirm their importance.

Experiment, which is at the present time of such far-reaching value, and which has led to such important disclosures in the investigation of infectious diseases, can, of course, not be employed in the investigation of tabes.

But clinical observation also presents very great difficulties in a disease which is so slow and insidious in its development, the beginnings of which are almost unrecognisable even by the patient himself, and often date so far back that the most important facts may have been forgotten (especially as the patient does not at first know to what they are due).

The only method which can lead to any result is a patient and careful critical collection of, if possible, a large number of isolated observations on tabes with reference to the previous lesions, and the importance of the facts thus ascertained can only become obvious through a statistical investigation.

The statistical method is in this case nothing but the employment of known inductive methods upon the case in point, and a very slight knowledge of inductive research is shown when individual authors will not utilise statistics in such an investigation.

It is an absolutely indispensable method in etiological re-

* See my Handbuch der Krankheiten des Rückemarks, 1st and 2nd editions, 1878.

search, as well as in other departments of medical science, even in pathological anatomy, and especially in a series of questions in which an experimental elucidation is not, or not yet, possible.

It stands to reason that useful results can only be obtained from statistics, if the latter have a correct basis; the individual observations must be exact, reliable, and critically sifted. Whoever does not take the trouble to ask his patients about the most important facts, who contents himself with their uncertain and superficial (indeed often dishonest) statements, who does not himself thoroughly examine and cross-question, can hardly claim either a hearing or attention upon this question.

Let us now turn our attention to the results of the recent clinical investigations.

The weightiest and most important result is most undoubtedly the fact of the perfectly overwhelming influence of syphilis upon the origin of tabes.

Having been engaged for the last 13 years in the investigation of this question, I have examined a very large number of tabic patients (now more than 600) in this connection and have already repeatedly published my results (7).

Briefly summarised, the result of my own statistics is, that, in so far as tabes in men is concerned, 89 per cent. have been infected by syphilis, of which 63 per cent. have suffered from secondary syphilis and 26 per cent. have been able to report the occurrence of a venereal sore only (without constitutional symptoms following). It is as good as certain that among those 26 per cent. of chancre cases a considerable number must be reckoned to the syphilitics; for example, all indurated sores and the not infrequent cases in which slight secondary symptoms were overlooked or forgotten.

There remain therefore only 11 per cent. of non-infected, and this percentage is probably a good deal too high, for among these many cases are reckoned in which a greater or less suspicion of syphilis was present (on various grounds), and very many where the patient had had one or more attacks of gonorrhœa, which may certainly not seldom mask a chancre.

For definite reasons I have repeatedly calculated the percentage of tabic patients taken exclusively from the lower classes. In the first series of 21 cases, the results were 85·7 per cent. infected, as against 14·3 per cent. not infected. A

second series of 50 cases, on the other hand, gave 76 per cent. infected, as against 24 per cent. not infected (in all, therefore, about 81 per cent. to 19 per cent.).

The reason why the number of the infected appears to be rather lower is quite apparent. The unreliability of the statements of patients of the lower classes is far greater than among the higher, and the non-recognition of lighter affections much more common; therefore syphilis occulta or ignorée is consequently more frequent.

And now, how does the matter stand with respect to tabic women? In them the proof of a syphilitic infection is, according to experience, ascertained with much greater difficulty. The disease often runs its course in them unnoticed and latent; there is possibly even a thorough contagion without the appearance of primary or secondary symptoms (by hereditary syphilis transmitted from the father to the fœtus), all points which must hinder our statistical investigation.

Of 32 tabic women observed by myself, 14 (=43·75 per cent.) were certainly syphilitic, 12 (=37·5 per cent.) in all likelihood were so, and in only 6 cases (=18·75 per cent.) could no previous infection be proved. If we add the first two figures together we obtain almost the same percentage as in men, and that in spite of the difficulties above-mentioned.

I will not go further into detail to show that these statistics suffer from the initial error of falling short of the true number of infected cases; this I and others have already often emphasised. For most frequently previous infection is concealed and obstinately denied; not seldom, however, one succeeds in convicting the patients of previous contagion by roundabout methods, through relations or the medical attendant, or by undeniable syphilitic traces.

I do not need to bring forward any examples out of the large number of cases I have seen. Many patients have forgotten the infection from which they suffered 10 to 20 years before, or they entirely overlooked it, having noticed nothing. I only need to remind you of Jumon's reports (8) on "Syphilis ignorée," in which he asserts that he has diagnosed unnoticed infection in the secondary stage as follows:—In men, 5 per cent.; in women, 20 per cent.; and in the tertiary stage as many as 17 per cent.; relatively, 50 per cent. We must also

remember the interesting reports of Fleiner (9) on syphilis occulta, which show how often syphilis exists without the patients having the slightest suspicion of how or when they were infected. Then again there is the possibility of hereditary syphilis, which is also, as a rule, unsuspected.

You see, Gentlemen, that all these well-known facts go to show that perhaps more than 89 per cent. of syphilitic patients may exist among those who suffer from tabes.

You must not, however, think that I alone have found such a large number. If I here bring forward my own experience I can also point to an imposing series of statistics given by others, which yield exactly the same results. Naturally, we can only take into account as valuable the newer statistics based upon the recognition of the object in view. Those which are based upon the histories of old cases—notes out of old case-books—or those which deal with too small a number of cases, are quite worthless.

In this connection Fournier found (in 249 cases) 93 per cent. syphilitic; Voigt, a former opponent of the relation between tabes and syphilis, found in 1881 67 per cent., in 1883 81·4 per cent., and finally in 1885 82 per cent.; Rumpf (19) found in 1883 66 per cent., and in 1887 85 per cent.; Gowers found in 1881 70 per cent., and in 1889 speaks of from 75 per cent. to 80 per cent.; Georg Fischer mentions at least 72 per cent., but probably as many as 90 per cent.; Labbé found 93 per cent.; Martineau as many as 95 per cent., and Dejerine 97 per cent.; Eisenlohr 60 per cent.; Bernhardt, at first 40 per cent., then 60 per cent., then about 58 per cent., and at last 83 per cent.; Althaus in 1881 90·6 per cent., and in 1884 86·5 per cent.; Remak in 1884 63·5 per cent; Seguin 72 per cent.; Spitzka 80 per cent.; Strümpell some 90 per cent.; Minor 60—70 per cent.; Hirt (in 319 cases) in 1891 92 per cent.; Gerlach (Hitzig's clinic, 1890) about 78 per cent.; Ferras in 1891 91 per cent.; Gajkiewicz in 1890 90 per cent., and so on.

At the same time, I will not conceal the fact that in some recent statistics much smaller numbers of patients previously syphilitic are given; thus Ballet and Landouzy appear to have found only 26 per cent.; A. Eulenburg 36·8 per cent.; G. Hofmann about 37 per cent., and Petrone over 48 per cent. of such cases.

I will not to-day examine the grounds for this remarkable difference, as Möbius justly remarks negative results are not so important as positive ones. It appears to me, however, incomprehensible that some observers should obtain such a different percentage from that which occurred in my own practice in more than 600 cases during the past 12 years, as well as in that of Fournier and others. After the progressive increase in the percentages which experience has shown us (see Voigt, Rumpf, Bernhardt, and others), it is certainly to be expected that the lower percentages of syphilitic patients will more nearly approximate to the truth, as care and experience increase amongst the observers.

Extraneous statistics concerning tabic women are rare: there are two series by Möbius (10), in the one, of 5 cases, 80 per cent., and in the other, of 13 cases, about 93 per cent.; and there is one by Minor (11) on 8 cases with 100 per cent. Here the results agree with my own.

My statistics show that the time when symptoms of tabes first appear after syphilitic infection are as follows: 75 per cent. of all cases occur in the first 15 years, and 88 per cent. in the first 20 years. Therefore tabes follows the previous specific infection within the subsequent 15 to 20 years.*

These statistics are indeed of themselves sufficiently convincing, but they would not be decisive, as we do not yet know how frequently syphilis otherwise occurs amongst the adult population.

Let us then make a counterproof. This consists in a statistical examination as to how frequently a syphilitic infection is met with in male adults over 25 years of age, suffering from disease, but who have not tabes and also do not suffer directly from syphilis.

* The exact numbers in the last 500 cases which I have published (among them 446 cases of patients who were infected by syphilis) are as follows:—

Tabes occurred between the		1— 5 years	in	63	cases.
,,	,,	6—10	,,	167	,,
,,	,,	11—15	,,	112	,,
,,	,,	16—20	,,	56	,,
,,	,,	21—25	,,	23	,,
,,		later	,,	10	,,
,,		unknown	,,	15	,,
				446	

I have now at my disposal a series of 6,000 cases of this kind from among the better classes. Of these it is found that only 22·5 per cent. were previously infected (about 12 per cent. with syphilis and 10·5 per cent. with an ulcer and in whom no secondary symptoms were remarked). A very striking result indeed! In the one case, in tabes, 89 per cent.; in the other, not tabic, 22·5 per cent., *i.e.*, in the former four times as many as in the latter.

Although it is to be presumed also in these statistics that the number of infected would be found too small, it is nevertheless likely, and indeed to be hoped, that the number 22·5 per cent. for adult males of the better classes is still too high, because it has to do with diseased men and because I have excluded dementia paralytica, &c. The number should therefore be further reduced, and in that case the 89 per cent. in tabes becomes of still greater importance.

The next conclusion then that may be deduced—at least in respect of the healthy male population—is as follows: that *almost all tabic patients have suffered from syphilis.* It follows then that hardly anyone runs a risk of becoming tabic who has not previously been infected by syphilis.

This expression "infected by syphilis," may here require a short explanation in which I must touch upon the subject of the unity or dual nature of the syphilitic virus. Unfortunately, this difficult question is not yet definitely decided; there are celebrated authorities on syphilis belonging to both the unitarians and the dualists.

I am of opinion that, even if the virus of the two forms of syphilitic sores are not identical or nearly related, the report that *only a soft sore* had been present does *not* permit the total exclusion of syphilis. That the *hard* chancre may be put down to syphilis without further question is certain, even if no secondary symptoms have been noticed, but there are numerous cases of so-called soft sores which are followed later on by secondary and tertiary symptoms. I have notes of several cases where, after apparently gonorrhœa with and without attendant buboes (urethral chancre?), secondary symptoms followed, so that all such cases may be looked on as giving a certain presumption in favour of the presence of syphilis.

If one also, at the same time, remembers the cases of syphilis

occulta and those where traces of former syphilitic infection are found in patients who have no knowledge of such manifestations, one is justified in speaking of a "syphilitic" infection, even in those cases where a "chancre" infection alone appears.

A further point which must be deduced from the foregoing statistics is that *a previous syphilitic infection is one of the most certain and necessary precursors of tabes.*

This will be all the more clearly apparent when we examine by statistical methods the *rôle* played by other pathological conditions in the etiology of tabes. I now set them forth individually:—

1. Direct heredity, *i.e.*, the transmission of tabes from either father or mother of the patient. This plays almost absolutely no part in the question we are dealing with.

I only found that the fathers of two tabic patients had suffered from tabes in 275 cases; one of these fathers had had syphilis, so had his son.*

I could ascertain nothing of the other case, where the son had had one gonorrhœa and glandular enlargement in the groins.

Again, the occurrence of tabes in brothers is exceedingly rare. I know of only two pairs of brothers who are tabic, but all four were also syphilitic.

This rare condition, definitely confirmed by Dejerine (12), *i.e.*, the rarity of several cases of tabes occurring in the same family, either in one or the following generation, appears to me to be the strongest proof against the supposition that a family predisposition or neuropathic heredity has a high importance among the causes of tabes. It completely overthrows the statement of Berbez (13), at any rate for the relatively early (before 30) patients attacked by tabes, that "a tabic patient comes from a tabic patient, or what is nearly the same, from a paralytic."†

2. The so-called neuropathic diathesis. Here also I only found 77 (28 per cent.) cases among 271, very few indeed as against the enormous frequency of this condition amongst the higher classes. It also seems to me to be exaggeration to speak

* This was also the case in Goldflam's experience (14); father and son tabic, both also syphilitic, we cannot call this hereditary.

† Amongst the 14 cases upon which Berbez bases his observations, are two in which father and son were tabic; in one case nothing respecting syphilis in either father or son is reported; in the other case, the son was syphilitic. This statement is sufficient.

of a neuropathic diathesis in cases where some nervous disease may perchance have attacked a distant relation.

3. It is easier to attribute to personal neurosis a greater influence when that condition was present before the onset of tabes. I found this state of matters in about 42 per cent. out of 251 of my cases. But patients' statements on this point are unreliable in most cases, as they attach very different meanings to the word "nervous."

Nevertheless a certain amount of influence must possibly be allowed, to judge from these statistics, but such conditions are now-a-days so frequent that one could obtain a similar percentage of "neuropathic diathesis" in patients suffering from a cold in the head or diarrhœa.

Here once more confirmatory proof fails! In my opinion, it is incumbent on those authors who place this condition in the forefront to carry out these confirmatory investigations; the result would surprise them.

It is chiefly the French school of the Salpetrière that has placed this question of heredity—the "famille neuropathique"—in the forefront. Under Charcot's auspices, Ballet and Landouzy (15) have worked up the subject, and in an imposing series of 138 (!) cases have certified that no other cause than nervousness and syphilis could be proved—

In	61 cases	...	50·8 per cent.
Definite syphilis alone in	21 „	...	17·5 „
Nervous heredity alone in	28 „	...	23·3 „
Syphilis and nervous heredity together in	7 „	...	5·8 „
Definite syphilis and probable heredity in	3 „	...	2·5 „
Total	120 „	...	100· „

The percentage is reckoned upon the 120 cases.*

From these figures, and upon further consideration, the author concludes that the nervous diathesis is the "predominating, sufficient, and possibly indispensable" cause of tabes! An astonishing conclusion indeed! It appears to me that these

* Unfortunately the numbers given in these statistical reports are full of errors, and one cannot understand them. In the Arch. de Neurol., in table 1, 105 cases, in table 2, 37 cases = 142 (instead of 138) are given; in the total from both only 120 have remained. Möbius gives 101 cases in table 1. In the Gazette des Hôp. (No. 8, 1884) it is said that out of 138 cases, 61 are of unknown origin, 36 hereditary, 35 syphilitic, 7 hereditary and syphilitic, and 3 are syphilitic and probably hereditary; this again makes 142 cases. According to this the percentage would again be changed.

statistics, which are certainly incorrect in respect of syphilis, simply show that neither syphilis nor the nervous heredity is the chief cause of tabes, as they both together are not proved in 50 per cent. of the cases, or they would both be at least approximately distributed.

Fournier has also protested strongly against this view and compiled a table according to which he could only point to 25 per cent. of cases with a nervous heredity; in 75 per cent. nothing of the kind was proved present.

In 61 cases Möbius found only one with tabes in the same family, and only 6 (=10 per cent.) with other nervous diseases. Oppenheim in the same way found only 10 per cent. with nervous heredity; Voigt in 165 cases only 15 (=9 per cent.); Rehlen in 35 cases 5 (=14·3 per cent.); Minor demonstrated the rarity of tabes amongst Russian Jews, notwithstanding their highly nervous diathesis. These facts will probably place Ballet and Landouzy's opinions at their proper value.

4. Chill is by some few thought to be the chief cause of tabes, I have only met with 34·5 per cent. (in 278 cases). If one considers how the public is apt to attribute everything to chill, how thoughtlessly chill is, as a rule, considered to be the cause of all illnesses, one must admit that the above percentage is still too high.

There is probably no doubt that one severe chill, or repeated chills, may develop tabes, or the long-continued influence of cold or damp workrooms or places and cold damp bedrooms may at times be blamed; but from this fact to the declaration of chill as almost the exclusive cause of tabes is a very long step.

5. Fatigue. I find this cause only given in 27 per cent. of 279 cases. To this class belongs the great fatigue of long journeys (exploring), or that experienced during hunting and war or manœuvres, &c., and it may be that we should add over-fatigue at the sewing machine or other similar employments.

6. The number of cases attributed to sexual excesses amounts to only 15·8 per cent. (in 271 cases), a very small percentage as compared with Romberg's views. Such facts are difficult to ascertain and are often concealed. Masturbation hardly comes in question, as the habit is only usual in early youth; but in a few cases in adults its etiological value has appeared to me probable. I think, however, that there is no doubt of the

importance attaching to sexual excesses, in cases where the first symptoms of tabes have occurred in young men during or shortly after the honeymoon, or where older men of about 50 have become tabic soon after marriage at that age.

7. Injuries play a certain *rôle* in the etiology of tabes, but only in rather more than 5 per cent. of the cases. At any rate, several cases have come before me where the initial symptoms of tabes have occurred after an injury—*e.g.*, after a broken leg, fall from a horse, severe shake, or after repeated shakes for years, &c.

8. Insufficient data are before us concerning the importance of the abuse of alcohol or tobacco. I find the subject mentioned in 18 per cent., a number which, owing to the frequent abuse of these luxuries, is not large enough to allow the attributing of a causative influence to them with any certainty.

9. The same may be said with regard to overwork, excitement, or emotion. I have not an adequate amount of material at hand, but at the same time I have had my attention called to these factors by 55 patients themselves, and have good ground to believe that, in conjunction with syphilis, they may possess a considerable influence in the development of tabes.

I know of no other conditions of any great importance to which I should direct your attention; but with regard to acute diseases as causing the development of tabes, I may point in a word to influenza. I have, as a matter of fact, noticed a distinct advance in tabes after patients have recovered from that disease.

These, gentlemen, are the chief definite facts which statistics yield us. If we glance at them again and summarise them, we see that the outbreak of tabes is preceded in nine-tenths of all cases by syphilitic infection; in about one-tenth by chill; in one-quarter by fatigue; in about one-sixth by sexual excess; and, finally, that about one-third of tabic patients spring from neurotic families.

If we are not prepared to accept the fact, without further proof, that by far the most frequent preceding lesion to tabes—in fact, the one existing in almost all cases—is syphilitic infection as the sole exciting cause, it appears that the disease is due to the combined action of various causes. Probably in the majority of cases this is so.

In order to recognise more exactly the importance and value

of the various causes inducing the disease, and to weigh one against another, it will be useful to investigate the question as to whether, indeed, each of these factors does solely induce tabes, and in about what frequency this may take place.

Here, again, a very convincing result becomes apparent from a series of 281 cases:—

Tabes was preceded by syphilis* alone in	27	per cent.	of the cases.
,, ,, neuropathic diathesis alone in	0·7	,,	,,
,, ,, chill alone in	1·4	,,	,,
,, ,, fatigue alone in	0·3	,,	,,
,, ,, sexual excess alone in	1·0		,,
,, ,, injury alone in	0·3	,,	,,

This table fully exemplifies the immense importance of syphilis. A pernicious condition which so much more frequently than all others together precedes the development of tabes must be of very special importance. On the other hand, it is obvious from this table that other pernicious conditions are almost only active when they are combined with syphilis, and only to be dreaded (in relation to tabes) by those who are previously infected by syphilis.

The relation between these conditions and syphilis is perfectly obvious in the following table of a series of 281 cases:—

Tabes was preceded by syphilis (*i.e.*, chancre) solely† in	77	cases ...	27	per cent.
,, ,, ,, and chill	32	,, ...	11	,,
,, ,, ,, ,, fatigue	17	,, ...	6	,,
,, ,, ,, ,, sexual excess ...	27	,, ...	9·6	,,
,, ,, ,, ,, injury	5	,, ...	1·7	,,
,, ,, ,, ,, neuropathic diathesis‡	31	,, ...	12	,,
,, ,, ,, ,, chill and fatigue ...	39	,, ...	13·5	,,
,, ,, ,, ,, chill and excess ...	5	,, ...	1·7	,,
,, ,, ,, ,, fatigue and excess	2	,, ...	0·7	,,
,, ,, ,, ,, various morbid conditions	11	,, ...	4·0	,,
,, ,, ,, ,, injury and chill or fatigue	3	,, ...	1·0	,,
	249	cases with syphilis.		

* In a former table with 100 cases the percentage was greater (36 per cent.), probably because I had then not taken into account the neuropathic diathesis; the remaining percentages are almost identical, only slightly larger.

† Amongst them, over 60 cases in which, notwithstanding the closest enquiry, none of the other conditions could be proved.

‡ This table does not contain, as Möbius rightly points out, all the cases with neuropathic diathesis. I have called attention here only to the most important points; anything further would have made the table too complicated; it is only intended to present a comprehensive picture, showing the relation of syphilis to the remaining conditions *in praxi*. The 25 or 30 cases of neuropathic diathesis

Neuropathic alone in	2 cases	...	0·7 per cent.
Chill alone in	4 ,,	...	1·4 ,,
Fatigue alone	1 ,,	...	0·3 ,,
Sexual excess alone	3 ,,	...	1·0 ,,
Chill and fatigue alone	2 ,,	...	0·7 ,,
Injury alone	1 ,,	...	0·3 ,,
Several causes (3—4) without syphilis	4 ,,	...	1·4 ,,
Cases, cause unknown	15 ,,	...	5·4 ,,
Total	32 cases without syphilis.		

A similar table of 100 cases, which I published in 1883, gave practically the same percentages.

These tables, gentlemen, will not fail to make an impression upon you; as a matter of fact, it is clear to every thoughtful person that no doubt whatever remains of syphilis being by far the most important and most frequent pernicious condition which comes into consideration with respect to the origin of tabes. Although this is so, it does not follow that anything definite is said as to the way in which this condition acts, and how the preceding syphilis is to be considered in respect to the subsequent tabes.

This is the vital point in the whole question, the decision of which is yet under discussion, and it may not be possible at present to arrive at one with certainty.

Two views are possible on the point: one (*a*) regards syphilis only as a predisposing cause, weakening the organism, especially damaging the spinal cord, and thus rendering the action of other causes possible; the illness induced will not be specific, but of an indifferent nature. The other view (*b*) is that which sees in syphilis the originating cause, which attacks the spinal cord directly, and is only exactly determined and localised in that organ through the other pernicious conditions; the ensuing illness would then be regarded as specific, or at any rate directly induced by the syphilitic virus, in fact a late form of syphilis.

From these views then the following questions arise: Is syphilis only a predisposing condition, or is it the true cause of tabes?

Already on general logical grounds the answer can hardly be doubtful.

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which are missing from the table would be divided under some eight heads, so that the percentage would not be much altered. As I have given above the exact percentage for the neuropathic diathesis, the small inaccuracy in this table may be excused.

From the concurrence of a larger number of different causes, among which one is specific while the remainder are of a quite different and very various nature, and from the greatly predominating frequency, indeed almost constant presence, of the specific cause, there is a very great probability that the specific is the active cause, and that it determines the character and the existence of the disease. Even if one only acknowledges a predisposition, its limitation to the single definite fibres in the spinal cord would again really lead to a specific influence. In this way, the conclusion is at once arrived at that tabes is a form of late syphilitic disease, or at any rate a sequela most closely related to syphilis and intimately connected with the condition following that disease.

This idea is strongly held by most of the authors who have given their opinion upon the subject, even when diverging views are taken of the way in which this intimate relation acts.

I may here be permitted to set forth a series of clinical facts which uphold this close relationship and the specific nature of tabes.

First, as regards the way in which tabes follows syphilis at certain regular times; it occurs at a definite interval—from 3 to 10 or 15 or at the most 20 years after syphilis—from which it follows that if syphilis is acquired late in life tabes occurs late also. The following are observations of my own on the subject:—

Infection at 48, tabes at 58 years of age.
„ 57, „ 66 „
„ 54, „ 59 „
Rumpf gives—
Infection at 48, „ 54 „
Voigt gives—
Infection at 55, „ 57 „
„ 55, „ 58 „
O. Berger gives—
Infection at 68, „ 70 „ and so on.

On the other hand, if syphilis be early acquired, tabes follows at an earlier age, *e.g.*, infection at 19, tabes at 22; and the cases of tabes in children, due to hereditary syphilis, must be taken into account (see the observations of Fournier, B. Remak (16), Strümpell (17), and Gowers).

Further, the occurrence of tabes during acute syphilis (case by Nonne) and the presence of syphilitic symptoms in cases of

tabes of some duration must be mentioned. This not very common condition has been proved by numerous cases seen by myself and also by other observers (see Rumpf, Fournier, &c.).

Then there is the presence of unrelated symptoms of nerve syphilis during tabes, and here the very frequent occurrence of paralysis of the muscles of the eye must be noticed. Every experienced oculist knows that these very common conditions in their various forms are nearly all attributable to syphilis, and Minor (18) has just recently published an interesting article to prove that the paralysis of the eyes so frequently seen in tabes is no true tabic symptom but rather a symptom of true syphilis. In the forefront of this part of the subject must also be classed the hemiplegias and paraplegias in the premonitory stage and during the progress of tabes, thought by many to be true "tabic" paralysis, but shown by Minor in a convincing way to be really syphilitic. To these symptoms must be added the cerebral symptoms and nocturnal headaches, &c., found at times in tabic patients.

Again, with respect to the proportion between men and women afflicted by tabes, tabes is known to attack men 10 to 15 times as often as women, and the same frequency (10·1) was found long ago by Fournier as regards syphilis in men and women.

Then there is the fact that in women of the higher classes tabes is very rare, just as syphilis is, whereas in women of the lower classes both diseases show a much greater frequency.

Further, the interesting fact of tabes in husband and wife, both syphilitic, has often been noted by me, as also by Voigt, Strümpell, Goldflam, and others. Tabes in a non-syphilitic married couple does not appear to exist.

Once more, the exceeding rarity of tabes in girls should be noted. A definite case of this has not yet been observed, although it would be possible for a girl to suffer from syphilis (not contracted per coitum) and consequent tabes.

Lastly, there is the fact established by Minor (11) that both tabes and syphilis are far less frequent in Russian Jews—who are highly nervous—than in the general Russian population.

All these circumstances, although they appear to support the syphilitic nature of tabes, are by no means perfectly conclusive and admit of many objections, although unimportant ones.

It is therefore only natural for us to turn to pathology and from it to seek an answer to the question as to whether tabes is a true syphilitic disease or not.

But in this case pathology has to encounter unusual difficulties. The question has only recently been asked in earnest and its discussion has but just begun. The material is not easily dealt with (*spröde*) and few investigations have been made with this object in view. More exact researches have yet to be carried on, and we know very well how important it is for the observer to direct his attention to definite points.

Some pathologists claim that pathology should give the final verdict as to what is syphilitic and what is not (specific or non-specific), but this claim appears to me to be as yet unjustified.

With the knowledge and methods employed at the present time by pathology, it is not possible to say with any certainty what syphilis is and what it is not (in contradistinction, for instance, to tuberculosis or leprosy).

Even the knowledge which pathology feels sure of—*e.g.*, that gummata or endarteritis is specific—*i.e.*, syphilitic—it owes to clinical observation and statistical proof that such lesions almost always occur in individuals who have previously suffered from syphilis. There are very few absolutely certain anatomical and histological characteristics in these conditions. Therefore pathologists should not continue to resent the fact that things which they regard as certain should be looked upon by clinical observers as specific-syphilitic and relegated to further pathological investigation.

It seems that among these things are the anatomical changes in tabes. What is already known of the pathology of this disease is probably as follows :—

The typical change is no doubt the grey degeneration of the posterior column of the cord, and, indeed, of a definite part of it. It is apparently a primary degeneration of the nerve fibres with an overgrowth of neuroglia occurring at the same time or subsequently, together with frequent thickening of the vessels, which, however, is not always present.

On the other hand, those changes which are usually stated to be specific-syphilitic are not usually found—no characteristic alteration in the vessels, no cellular infiltration of the adventitia or of the meninges, no gummatous changes, &c.

The expectation which was held for a time, especially after the investigations of Adamkiewicz, that tabes might possibly originate from a primary change in the vessels, and that the diseased condition of definite parts supplied by the vessels depended upon the typical localisation in the posterior column, has not been fulfilled. Apart from the fact that the expected alteration in the vessels is not found in most cases, the localisation of the tabic degeneration is also quite different from that of the areas supplied by vessels. As Flechsig has recently demonstrated with great certainty, it rather attaches itself pretty closely to the fœtal decussation of the posterior columns. It is also essentially caused by the disease of definite nerve tracts, and cannot, indeed, be well attributed to any possible syphilitic disease of the arteries of the spinal cord.

It may therefore be said that the grey degeneration of tabes is a thing by itself and different from the alteration in the vessels, with its results on the nerve substance, such as meningitis and the like, now believed to be specific, which one cannot at present say with regard to the grey degeneration of tabes.

Is it, however, on this account really not specific after all?—*i.e.*, a lesion developed and really caused by syphilis.

So far as I see, there exists no serious reason why the answer to this should not be in the affirmative.

It has already long been a much-discussed and growing idea that syphilis in the nervous system, together with the so-called specific lesions due to proliferation of cells and infiltration, especially in the connective tissue and vessels, and also another series of disorders, can of itself develop degenerative changes in the nerve elements. It is supposed that this depends upon a distinct form and kind of the syphilitic action, and that the proliferation of cells is due to the direct action of the cause of the syphilitic disease (bacteria), the primary degenerations of poison (toxine) which are produced by this cause of the disease (syphilo-toxine).

Attention must also be directed to the question as to whether both series of changes in tabes are frequently found together or not. If they are, this would naturally be in favour of the syphilitic nature of tabes; whereas, if such an occurrence is rare, it would not prove much, because such series of appearances

may belong to different stages and periods of the development of syphilis, and from the fact, for instance, that condylomata and gummata are, as is well known, seldom seen together, one cannot conclude that the latter do not arise from syphilis.

As a matter of fact, now that great attention is directed to the matter, cases increase in a striking manner in which both kinds of changes are found side by side, leading more and more strongly to the conclusion that the simple atrophic and degenerative changes in the nerve elements may be developed by syphilis.

For example, there have been observations in which the typical grey degeneration of the posterior column has been found in tabes together with the "specific" changes in the vessels—syphilitic meningitis, gummatous infiltrations, nodules, &c. I have two cases of this kind in my mind now of recent date; the one refers to a case already described by J. Hoffmann (20) and Sydney Kuh (21); the other, a perfectly analogous observation, will be published shortly; and to these must be added four observations by Marinesco (22), Minor's case (18), and the recently published (1891) observation of Eisenlohr (23); also Brasch's (24) observations.

There are also the cases where, together with widespread "specific" syphilitic disease of the central nervous system and the meninges, the commencement of typical tabes is found, as in the highly interesting case of Oppenheim's (25), where, together with well-marked syphilis of the spinal meninges and roots, in the dorsal region and in the vessels, &c., there was found in addition complete tabic degeneration of the nucleus and fibres (also clinically the complex symptoms of "bulbar" tabes). In the same way, in the second case published by Eisenlohr (26) in 1889, where, in addition to syphilitic cerebro-spinal meningitis, a symmetrical degeneration in Burdach's column, analogous to that seen in tabes, was found, from the medulla oblongata to the middle of the dorsal region of the cord; finally, the third case of Marinesco may be here included.

As further proof, those cases are useful where other degenerative atrophies (without degeneration of the posterior column and with or without a specific-syphilitic disease at the same time) must, notwithstanding all scepticism, be referred to syphilis, such as atrophy of the bulbar nucleus and nerve tracts,

especially the nuclear degenerations of the nerves of the muscles of the eye. The observation of Oppenheim previously referred to, and the important cases of Siemerling (27) in his large work on the chronic progressive paralysis of the muscles of the eye, are here of the greatest interest.

If this explanation—which can hardly be questioned—be allowable and correct, and if in other cases of notoriously syphilitic patients both series of changes are found side by side, —the gummatous, the meningitic, and the endarteritic on the one part, the simple grey degeneration on the other—why should one only be specific and the other not? Why should the one be developed from syphilis and the other not?

And if we find the same grey degeneration of the posterior columns by itself so regularly in former syphilitics, why should we make a point of rejecting syphilis as a cause of this same degeneration in tabes?

There is no reasonable cause for this. We must learn to place these conditions in close connection with syphilis. Do we not see in other organs of the body (in the liver, lungs, vessels, bones, &c.), together with syphilitic changes, those also occurring which do not appear to be at all specific, but which nevertheless are generally considered to be caused by syphilis?

Neither do analogies fail us here. Tuberculosis, the infectious disease apparently most nearly related to syphilis, induces very various pathological changes (miliary tubercle, caseous bronchopneumonia, interstitial pneumonia, lupus, &c.), whose etiological relationship is certainly proved; indeed, in multiple neuritis they produce also generative atrophy of the nerve tracts. Diphtheria in the same way induces in the nervous system a whole series of various forms of disease—inflammation, cellular infiltration, hæmorrhagic degeneration, degenerative neuritis, &c.—all certainly having a common origin. Chronic alcoholism too calls forth, as does syphilis, vascular disease, endarteritis, &c., as also degenerative changes in the nervous system (grey degeneration of the spinal cord, cerebral degeneration, multiple neuritis, &c.).

In addition to this, we know that the syphilitic alterations in the vessels which are held to be truly specific show a very great resemblance to the diseases of the vessels due to other causes (alcohol, lead, gout, &c.), which are nevertheless generally held

to be due to a specific cause. Why then shall grey degeneration only in syphilitic individuals *not* be specific, because they also have a great resemblance to grey degeneration of a different origin?

Even the fact, so frequently insisted upon by the opponents of the foregoing view, that in tabes we are concerned with a "systematic" disease and that such a one can hardly be induced by syphilis, supports very distinctly the specific origin of the disease, as, besides myself, Möbius (10), Strümpell (28), and others have often pointed out. If in this case we have to do with a specific poison, it certainly almost stands to reason that the poison acts in a very special way upon definite nerve tracts and systems, which undoubtedly have their specific peculiarities and affinities. It is unnecessary to fog the subject with toxicological and pharmacological facts!

But in the consideration of this subject, we possess the most striking analogy in pathology in the so-called post-diphtheritic ataxia and paralysis. We see a perfect reflection of tabes, although in an acute and curable form—pupil phenomena, ocular paralysis, disturbance of sensibility, absence of reflexes, ataxia, induced by a bacterial disease which evidently in part injures the same anatomical tracts as tabes, but in an acute, not progressive, and curable manner; an "acute tabes," so to say, caused by an acute bacterial unprogressive disease, in contrast to the chronic progressive true tabes induced by a chronic bacterial disease (syphilis).

In ergot poisoning—in all probability an intoxication also due to low vegetable organism—we see, as Tuczek (29) has shown, a grey degeneration of the posterior column, and this occurs with symptoms not unlike those seen in tabes, which, if not possessing full identity, certainly present a far-reaching analogy with the degeneration of tabes.

These things then indicate in a striking way the possibility and probability that an analogous disease can also be induced by syphilis.

From all these considerations, gentlemen, we may deduce the conclusion that pathology has not up to the present given a definite decision upon this question, but we can say with certainty that there is no definite pathological change apparent in this disease which goes against the theory of a specific origin of

the same. It is very possible, indeed in the highest degree probable, that the typical grey degeneration seen in tabes is the result of syphilis.

When we summarise all that has been said, we must come to the conclusion that in the majority of cases tabes is most probably to be considered as a direct sequela of syphilis, as a manifestation of syphilis belonging to the third stage of the disease.

But now arises the far more difficult question: In what way are we to regard this manifestation? In what relationship does it stand to the other manifestations of tertiary syphilis? On this point various views have already been brought forward.

Fournier treats post-syphilitic tabes simply as a specific tertiary affection, and regards it as quite natural that tertiary syphilis should appear as "selerosis" in the spinal cord, as indeed it may appear in all other organs, together with gummatous changes.

I have always confined myself to the elucidation of the fundamental facts, and cautiously avoided a definite opinion concerning the kind of relationship that exists between tabes and syphilis, but I have never concealed my opinion that it is probably right to consider tabes as a late manifestation, a specific result, of syphilis.

On the other hand Möbius (10) and Strümpell (28) have endeavoured to explain, by the consideration of new views, the difference between the pathological lesions of tabes and the specific gummatous changes, and so to reconcile the clinical facts of the etiological relationship of tabes and syphilis with that anatomical difference.

Möbius first explained tabes as a sequela of syphilis, but not as equivalent to tertiary lues. But to this must be remarked that the whole of tertiary syphilis has for long been regarded by many distinguished syphilographers as a kind of subsequent disease to syphilis, but having no further connection with the syphilitic virus as such.

At almost the same time, Strümpell also put forth the idea that in tabes we have a nervous disease following on syphilis, which he compared in a detailed manner with the similar sequela of diphtheria. He took a chemical poison as origin of the degeneration of tabes, a product of tissue change induced

by the syphilitic virus, a kind of hypothetical syphilo-toxine, which had a degenerating influence upon the nerve elements in a similar manner to lead, arsenic, ergot, or as a ptomaine produced by either diphtheria or any other infectious disease. To him therefore tabes is a post-syphilitic intoxication.

Rumpf issued a polemic against the acceptance of this toxine, and is inclined to believe in the acceptance of small syphilitic changes induced direct from the virus at the primary foci of disease.

On the other hand, Möbius agrees with Strümpell's hypothesis, and, even when a syphilo-toxine remains, regards tabes in all cases as a sequela of syphilis, or upholds very decidedly, as he recently said, that it is a "meta-syphilitic" disease, leaving, however, the manner of the relation between the original and subsequent disease still undecided.

These, on the whole, very plausible views are, however, still without a firm basis. We do not know anything in detail either of the bacteria which cause syphilis and of their vital qualities, or of the products of tissue change which they induce, or the possible action of these. Only after this hiatus has been filled can a serious explanation of these difficult relations be thought of. Indeed, we may already, considering the enormous number of facts established by bacteriology, recognise the possibility of explaining the symptoms of syphilis by the hypothetical acceptation of bacteria and their action.

In an interesting and stimulating work, E. Finger (30) has sought, and with effect, to show that a very striking part of the appearances of syphilis in all stages is found in the products of tissue change of the syphilitic bacteria (of the real virus), and he specially tries to prove that the tertiary appearances stand in a very intimate connection (Causalnexus) with these products of tissue change (syphilo-toxine). If they only act in a limited degree, they should cause the immunity of the organism from syphilitic infection; but if their action is stronger, they produce a greater alteration in the reaction of the organism, a kind of specific cachexia, really a malady which is a sequela of syphilis, during which the most different irritations and symptoms—perhaps even some still remaining syphilitic virus itself—can "auslösen" (?) this pathological reaction of the organism, and so produce the tertiary symptoms.

It is certain that only the ordinary symptoms are mainly intended here—that is, the gummatous and related lesions. In these, Finger recognises the prompt reaction of iodine as characteristic. He does not go further into the other possible tertiary changes, especially the degenerative atrophies of the nerve tracts, neuritis, grey degeneration, &c., and the many causes of their difference, and that is for us just the most important point.

Finger endeavours to explain the continued existence of these post-syphilitic actions, which occur even when the syphilitic virus has long disappeared from the body, by reference to known chemical "Kontaktwirkungen" (?), according to which the toxine, during its chemical influence on the continually regenerated substance of the organism, has the power of always reproducing itself, and so always keeping up its action, even when the virus which engendered it has already disappeared.

However alluring these deductions may be, however many handles they afford for the clearing up of the connection between tabes and syphilis, we must nevertheless not forget that they are to a great extent still hypothetical, and concern a territory which, through the confusing variety of its appearances, presents the greatest difficulties to scientific knowledge, so that we must desist from at present giving a fully-satisfying pathogenesis of tabes as resulting from syphilis.

But still it seems to me that so much is proved—that in the majority of cases tabes is an indubitable result of syphilis; that certainly tabic degeneration is something different from the usual tertiary form of syphilis; but that this admission does not prevent the possibility of this degenerate form being also a result of syphilis.

And then it really seems most plausible to regard this degeneration as the action of a poison, as being brought about by the products of tissue change of syphilis, and to place it as a parallel case to other poisonous actions which lead to degeneration. It is especially instructive to notice the resemblance between this and post-diphtheritic disease of the nervous system. In the same sense as the latter is regarded as a sequela of diphtheria, but yet as intimately connected with the original local disease, can one look upon tabes as a sequel of syphilis, but also as a disease depending on the products of

tissue change in syphilis and as intimately connected with syphilis.

If we wish to follow the arguments brought forward by Finger, we should have to regard tabes as a disease depending on the products of tissue change of the syphilitic virus, which presents only one particular form of the tertiary disease. If with this the view agrees that the action of these products of tissue change is mainly only a reaction of the organism in respect of particular tissues, which only lead to real illness when certain irritating influences gain entrance, we should begin to understand why in many cases the entrance of other diseases is necessary in order to draw out the tabes; it would indeed then, in a certain sense, be a question of the "disposition" to the illness of certain nerve tracts caused by the action of the syphilo-toxine. Indeed, simpler and much more plausible seems the assumption that the action of the poisonous products of tissue change directly and primarily cause the degeneration of particular nerve tracts. But this might also apply to a quantitative difference in the action. The more powerful action of toxine might cause degeneration at once; while if it were weaker it might require the help of other causes in order to bring about the degeneration.*

After Finger's arguments we can quite well dispense with the assumption (till now always held) that under all conditions in the body there exists somewhere a latent centre of disease which contains the virus, and constantly produces afresh the products of tissue change, and we can understand why tabes, like other tertiary symptoms, often does not commence till so long after the primary illness. Also an explanation presents itself as to why persons not affected primarily or secondarily but who are "immunisirt" (?) through the products of tissue change (as for instance women who have given birth to children inheriting syphilis from their father without being themselves affected by the disease, cases of syphilis occulta, &c.) can suffer from tabes, to which fact Möbius has already drawn attention.

* The recent facts that stand out with greater and greater clearness showing that certain bacteria cause various products of tissue change, of which the one (the toxalbumine) acts merely "immunisirend" (?), the others (the bacteria protein) however with an irritating and toxic action, and which can be mixed in varying relations, are not taken into account in these considerations; the relation becomes only more complicated in view of these facts.

One could say much about this, but I will let this suffice with respect to these hypothetical arguments. And I regard it as still less opportune to go at present more particularly into the hypotheses and to discuss with Marinesco the question as to whether the toxic action in tabes really works on the nerve fibre tracts directly or only on the end of their trophic centres, so that the degeneration should be regarded as secondary. That question may be left for the present.

Now then, gentlemen, after all these considerations, we can hardly draw any other conclusion than that tabes originates in the great majority of cases from syphilis.

This conclusion throws a strong light upon a whole series of facts which, throughout the etiology of tabes, are especially referred to as general predisposing causes, viz., the almost exclusive occurrence of tabes in middle life (30 to 50 years of age), whilst syphilis is usually acquired between the ages of 20 and 30.

The majority of cases occur in men, because they suffer from syphilis far more often than women.

When tabes occurs in women it is seen more frequently in the lower classes than in the higher.

Possibly also the more frequent occurrence of tabes in those paths of life which predispose to syphilitic affections, but this can only be decided when a far greater number of cases is available for statistics.*

But even although we must acknowledge syphilis to be the

* In a table which I have recently published of 550 cases of tabes, we have the following results :—

Merchants (bankers, &c.)	207
Manufacturers	27
Officers (excluding medical officers)	50
Railway officials, engineers, architects, &c.	39
Lawyers, &c.	34
Medical men (civil, military, dentists)	26
Literary and artist classes (professors, teachers, chemists)	24
Landed proprietors and factors, &c.	20
Hotel proprietors, brewers, &c.	19
Gentlemen (unemployed)	13
Clergymen	1
Artizans of all kinds	42
Workmen, farmers, day labourers	30
Police, soldiers, fishermen, railway porters, engine-drivers, &c. ...	18
	550

most important factor in tabes, I do not at all think of excluding the possible association of the other factors mentioned above. It is indubitable that the results of severe chills, fatigue, injuries, sexual excess, emotion, and maybe even the abuse of alcohol and tobacco, induce the outbreak of tabes in a whole series of cases, and it appears more than probable that the nervous diathesis frequently helps to bring on the disease.

Nevertheless, it must be again and again insisted upon that all these factors act chiefly and almost entirely in syphilitics and are only as a rule dangerous to them, so that we can only attribute to these factors an auxiliary importance. They determine, we might say, the outbreak of the syphilitic disease in certain parts of the nervous system, chiefly in the posterior part of the spinal cord.

In the history of the most various syphilitic manifestations such things are not unheard of. To recall only the causing of cerebral syphilis by great intellectual fatigue or excitement or injury to the cranium, the syphilitic disease of the skin brought out by cutaneous irritation of all kinds, slight wounds, suppuration, or syphilis attacking the liver in consequence of injury, &c.

Probably in such cases the matter may be considered thus:— That a certain debility, a slight disturbance in the nutrition of the nervous elements, is set up by the factors just mentioned, which elements then succumb to the influence of the syphilitic toxine, which has been present and slowly working for some considerable time, and begin to degenerate.

In the toxic diseases must also be considered the "superposition" of the poisonous actions, as has been urged by Oppenheim (31) and supported by interesting examples.

It is, indeed, not to be wondered at that these affections alone, especially if several act at once, are sometimes able to induce tabes, for it must be regarded as certain that *there are isolated cases of tabes without any previous syphilis.*

The 10 per cent. which still remain, after the most careful investigation and statistics, cannot be altogether eliminated or put down to syphilis, however far one may go in the acceptance of syphilis occulta, the syphilitic "Immunisirung," and of concealed and hereditary syphilis. I cannot follow Möbius in this matter when he refers all cases of tabes without exception

to syphilis, and wishes to define tabes as the offspring of syphilis. I entirely acknowledge his weighty reasons, and agree with him that it is an almost necessary logical conclusion to regard tabes as always based upon a post-syphilitic intoxication; but I also consider that Nature does not nearly always accept the most conclusive arguments that have been constructed by the clearest logical conclusions at the writing-desk. She goes her own tortuous way, which we have patiently to explore.

When, indeed, we see in how many cases of gumma in the throat (tonsils), for instance, a previous syphilitic infection is absolutely impossible of proof—Fournier found, at any rate, syphilis *ignorée* in 44 per cent. of such cases—and when, granting another possible cause of tabes, we must find it very wonderful that tabes without previous syphilis is not much more frequent, the correctness of Möbius's views are borne upon us more and more. It will please me very much indeed if future research proves in a convincing manner the truth of a connection so constant and without exception. At present, however, I do not feel compelled to accept this conclusion.

Gentlemen, I have finished. From what you have now learnt of the newest researches, the etiology of tabes certainly appears in rather a different light from what it did. We may say that we have made a good step forwards in the knowledge of the cause of tabes. Still, we are not quite at the goal. Apart from the fact that there are still isolated cases in which the most careful investigation fails to prove the existence of any of the causes that I have mentioned, we are not by a long way perfectly clear concerning the minute relationship between the etiological lesions and the pathological changes, and concerning the manner and way in which the pathological lesions arise. Nevertheless we appear to be on a solid foundation for further research to build upon.

It will be the work of the near future to obtain further light concerning this highly interesting scientific problem.

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THE TREATMENT OF TABES.

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TRANSLATED

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THE TREATMENT OF TABES.*

By Wilhelm Erb.

Gentlemen,

You have recently had the opportunity of seeing a large number of patients suffering from tabes, and we have gone so much into detail in the examination of the method of development of this remarkable disease, together with its very complex and varied symptoms, the many-sided character of its progress and its etiology, pathology, and diagnosis, that we have gained a fairly complete picture of it, which I hope will not soon fade from your memory.

You have heard that tabes is by far the most important and frequent of all chronic diseases of the spinal cord. Even the layman, at the terrifying words, "diseases of the spinal cord," as a rule, thinks of nothing else but tabes, the old "spinal cord consumption," with its fatal progress and end. It is a disease of great social importance, because, attacking usually men at the zenith of their life, it destroys the possibility of valuable power to work, whilst not proving fatal for many years; even, indeed, for tens of years. Tabes is a heavy burden for the patient, its weight being increased by its long continuance and uncontrollable progress.

No wonder, then, that this disease has been a matter of grave care to every earnest doctor, and an object of very numerous therapeutic experiments, although, unfortunately, with little success.

For tabes shares the fate of all forms of disease of the spinal cord which are classed under the name of chronic myelitis, "grey degeneration," and sclerosis—it resists, as they do, nearly all therapeutic efforts. Owing to its long duration and the exceptional fluctuations and variations in its course, it is more than usually difficult to collect satis-

* Elaborated from lectures given in my Clinic for Nervous Diseases. Klin. Vortrage, N.F., Nr. 150 (Innere Medicin, Nr. 46), April, 1896.

factory and definite therapeutic experience. It presents favourable and unfavourable, benign and malignant, tardy and rapid forms, which cannot be recognised as such from the outset of their appearance. On account of the tedious and often delayed action of certain therapeutic measures, the not infrequent necessary combination of several of these, and the often unexpected remissions and improvements in the progress of the disease, judgment as to its issue is rendered very uncertain. Not a few of the tabic symptoms are capable of being influenced by suggestion, and therefore the statements made by the patients on the results achieved are deceptive. All these points explain the fact that many different recommendations are made without good cause, and that numerous and often peculiar methods of treatment are tried and as quickly given up.

Our knowledge of the pathological basis of tabes affords us no sufficient ground for treatment; it is as yet much too uncertain and incomplete. The essential nature of the tabic process is still altogether unknown to us, and even the ultimate seat of the disease continues to be a matter of dispute. Do we not speak, not only of the posterior column of the spinal cord, but also of the spinal ganglia, the posterior roots, the peripheral nerves, the medulla, and even of other areas?

Not even a lucky chance has hit upon an empirical cure for this fearful disease, however thankful we would be for it.

There only remains to us the ever immovable foundation of all scientific treatment, namely, the more or less deep insight into the nature and progress, and especially the causes, of the disease. But that this insight as regards tabes is not very brilliant, you know, gentlemen, from what I have told you in former lectures. Recent times have, however, brought us great progress in this respect, although truly we are still far from the goal. Especially concerning the etiology of tabes, we have now much more certain knowledge than formerly, and I have previously summarised our present knowledge in this respect.*

In the following discourse, therefore, we will consider the therapeutic experiences which have been collected in the past years, together with the results of exceedingly rich

* The Etiology of Tabes. Samml. klin. Vortr. Neue Folge. Nr. 53, 1892.

clinical investigations and of pathological researches, especially the detailed established etiological facts given in the lecture I have alluded to, as a foundation and standard for the remarks here given.

It may be most useful if we at once go through, in order, the several indications before us, enumerate the means which may be employed with advantage, and critically examine their results, in order to gather from them the most important conclusions as to the treatment of the disease. This must inevitably take rather long.

I.

Gentlemen,—Let us turn in the first place to the question as to whether a *prophylaxis* to tabes exists. Owing to the great frequency of the disease, to the grave danger to which those attacked are exposed, to the progressive character of the symptoms, and the difficulty of treating them successfully, it would indeed be best in this case, as in all other diseases, if one could prevent the malady.

It is obvious that we can only speak of a prophylaxis for tabes if we more or less know its cause.

Gentlemen, *the causes of tabes are now known*, and we probably know sufficient of them to enable us to base upon them a rational prophylaxis.

As I showed at length in a former lecture—and proved beyond any possible doubt—that syphilis is certainly the most frequent cause of tabes, I do not need now to go into the details of that subject. I will only mention that since that time all the fresh and rich experience which has been gathered confirms, if possible, more strongly this opinion.

It appears to be really needless for me to produce further material, as all recent experience only confirms the former. As, however, there are still a few authors who are blind to the clear facts, or depreciate them, or throw doubt upon their correctness, I will give here a short summary. I have now at my disposal a new series of over 270 cases of tabes, among which are 25 from the lower classes and 9 women. Leaving these latter in the meantime, I have a progressive series of 200 *cases of tabes in men in the higher ranks of life*, who give

by far the most reliable previous history, especially with regard to syphilitic infection; other etiological factors I pass over for the moment. In these 200 cases I find—

(*a*) Cases in which there is no possible proof of syphilitic infection	15	7·5	per cent.
(*b*) Cases in which there was previous syphilitic infection	185	92·5	„
Amongst these latter, there were cases with definite secondary syphilis	123	61·5	„
Cases of chancre without noticeable secondary syphilis	62	31·0	„

It is to be noticed with regard to the 62 cases "only infected by chancre," that there are at least 25 in which it is noted that the chancre was "hard," or that it had been treated either by mercury or iodide of potassium, and therefore certainly considered syphilis by the doctor in attendance.

Of the 15 cases "not infected," 11 were not by any means unsuspicious (on account of one or more attacks of gonorrhœa, stricture, buboes, or because of the wife's frequent miscarriages, leucoplakia of the mouth, syphilis of the father, &c.), and therefore there were only 4 about which one could say with certainty—so far as it is indeed possible—that they were not syphilitic.

In 200 cases, then, there were only 2 per cent. in which no suspicion of syphilis could apparently be entertained.

These figures speak with no uncertain sound, and they also corroborate completely my former statistics concerning 500 cases: indeed, they are slightly stronger.

The total 700 cases—and there are not many investigators to be found who possess such a large and reliable series of cases observed according to a fixed principle—give 90·35 per cent. formerly infected (with syphilis or chancre) and 9·65 per cent. not infected.

I will add a few trifling facts in this connection. Among my new cases are again found two theologians who had been both syphilitic—one when a student, the other having been infected at vaccination. Further, three pairs of brothers; all of these (collectively and severally) had been syphilitic. Lastly, a married couple; the man had had a chancre 20 years ago, and now has leucoplakia of the mucous membrane of his mouth, and is, from his weak patellar reflexes and

other symptoms, suspected of having tabes. The wife has suffered from well-marked tabes for two years.

The 9 new cases of tabes in women are as follows: 6 of them had certainly had syphilis, 4 were infected by their husbands, 2 were puellæ publicæ; in 2 cases the husband was certainly syphilitic, and the women had aborted several times, and one, according to the formation of her own husband, had probably been syphilitic before marriage. Therefore, in 9 cases, 6 had certainly had syphilis, 2 almost certainly, and 1 highly probably. *Sapientia sat!*

For details concerning this statement, see Berlin Klin. Woch., 1896. No. II.

Together with syphilis, however, other factors play a certain *rôle*, for tabes is, in many cases, the consequence of the combined action of a whole number of morbid conditions, amongst which certainly syphilis is the most important, and, indeed, almost without exception present. Under these morbid conditions, the neurotic temperament takes the next place, a certain importance must be attributed to hereditary or acquired nervousness, and then there are further a whole series of "contributory causes," which, in those who have had syphilis—*and usually only in such*—may cause the onset of tabes.

These "contributory causes," as I have pointed out in detail in my former lecture, are: *severe chill, bodily fatigue and over-exertion, sexual excesses, sometimes injury, then abuse of alcohol and tobacco*, probably also *excessive mental work, overwork*, and possibly also *great excitement and emotion*.

It is therefore easy to say wherein the prophylaxis of tabes may be found.

By far the most important part of it is in the *timely, thorough, and sufficiently long treatment of syphilis* at its onset. I have nothing to say in detail concerning this. The rules for the treatment of syphilis, to ensure a proper and certain success, are now universally recognised. Would that they were everywhere carried out! But in this connection doctors fail only too frequently, often in a perfectly unjustifiable manner. Frequently the primary manifestations of syphilis are only locally treated, the treatment is omitted

when the first secondary symptoms have hardly disappeared, the patients are lulled into a false security by the assurance that it was only a "harmless" chancre, and "that all is cured," &c.

I could give a long list of such cases met with in my practice, in which, not only on the part of the patients—which, of course, often occurs—but also on the part of their doctors, in their treatment and supervision of syphilis, there has been perfectly unjustifiable thoughtlessness. I wish, gentlemen, to give you an earnest warning on this point.

Experience teaches here, as in cerebral syphilis, that it is not always the severe and intractable cases, but just those forms of syphilis which are apparently slight, that heal of themselves and quickly disappear, and that are on that account neglected and insufficiently treated, which are followed by tabes later on.

The thorough and comprehensive discussions of syphilographers during recent years have shown with increasing clearness that the more thorough and longer the treatment of syphilis with Hg. the more certain will be the prevention of the appearance of tertiary symptoms.

The statistics on this point from *Fournier*, *Neumann*, *Haslund*, *Vejda*, *Ehlers*, *Neisser-Marschalko*,* and others, and even those from *Jadasohn*† (whose sifting of the cases was most keenly critical), teach this unanimously and indubitably.

Certainly it may be here objected that it has not yet been proved that tabes is a tertiary manifestation of syphilis. That may—with all reserve—be granted. But that the same applies to tabes—that in regard to it a thorough and timely treatment of syphilis is of indubitable value, is taught by Fournier's‡ valuable statistics concerning the frequency of tabes after insufficient, after moderate, and after long-continued treatment of syphilis.

* For details see Th. v. Marschalko Beiträge zur Ätiologie der tertiären Lues, insves. über den Einfluss der Quecksilber-behandlung auf das Auftreten tertiärer Symptome. Arch. f. Dermatol. u. Syph., 1894.

† See Berioht uber d. V. Kongr. d. deutsch dermatolog. Gesellsch. zu Graz Berlin. Klin. Woch., 1895, No. 51. p. 1127.

‡ Fournier, Enquête sur la prétendue action tabétogène du traitement mercurial, &c. Gaz. hebdomad de Méd. et de Chir., 1891, p. 606.

From his rich experience, Fournier tabulates *321 cases of tabes with previous syphilis*, as follows:—

24	In which there was no treatment at all.			
70	,,	there had been absolutely insufficient treatment.		
103	,,	a 3 to 6 months' Hg. treatment was ascertained.		
74	,,	treatment had lasted 6 to 12 months.		
32	,,	,,	,,	1 to 2 years.
18	,,	,,	,,	2 to 4 years.
321				

According to this table of cases of tabes, the relationship between those cases (after syphilis) which had been neglected or insufficiently treated, or only treated for one or, at the most, two years, and those which had been thoroughly well treated for two to four years, is as 23 to 1. This leads to the indubitable conclusion, after critical examination of all possible objections (that is, for Fournier and all objective thinkers), *that a thorough anti-syphilitic treatment of the first stages of syphilis very considerably diminishes the chance of tabes following subsequently*, and also that the remarkable assertion put forth by some that the Hg. treatment (of syphilis) favours the subsequent outbreak of tabes is completely gratuitous and perfectly unfounded, for 24 of the above cases never had Hg. at all, and in 70 cases only minimum doses were given.

In addition, however, to this, Fournier's statistics set forth the unsatisfactory fact that even an energetic and long-continued treatment of syphilis by mercury is not certain to prevent a subsequent attack of tabes, but, as is well known, this fact applies to all the tertiary forms of syphilis.

It may certainly be said *that the best prophylaxis of tabes is to be found in a thorough and long-continued specific treatment of syphilis in its first stages.* Whether at the same time —as *Fournier's* pregnant and clear statement permits one to suspect—it is not also of importance during the anti-syphilitic treatment to pay attention to the possible consequences of the disease on the nervous system and by suitable methods which would serve to strengthen and guard that system, to repair it, will only be learnt after we have had much more and fuller experience. I shall have to mention these methods immediately.

In the first place, I will only point out how important the *prophylaxis of syphilis* itself is for our purpose: the less syphilis there is amongst the population the less tabes—that is obvious. But it is not now my task to deal with the subject of the regulation and examination of prostitutes, instruction of the interested persons, careful and strict treatment of syphilitic patients in hospitals, and possible legal action against unconscientious infection by the sick of the healthy, and other prophylactic measures.

Unfortunately, I cannot rid myself of the impression that in this province public hygiene and State care for the health of the people falls far short of their appointed task and is conducted to a great extent on lines very different from sanitary police principles. It is high time that a thorough change took place in this direction.

But, gentlemen, the treatment of syphilis alone is not of itself sufficient. We have learnt to know further a whole series of other factors, ascertaining however at the same time that they *nearly always only* come into action in those who have had syphilis; therefore syphilitic patients should be warned of these influences and protected against them, so that they may not later on fall victims to tabes. This is of especial importance for those individuals who show an *hereditary neurotic tendency* or possess an *acquired neurotic diathesis*. The number of these in the present day is unusually large. In these cases there is every reason to warn and impress upon all patients affected by syphilis to protect themselves in the first place from all severe or frequent *exposure to chills*, not to foolishly or needlessly expose themselves in hunting, mountaineering, boating, or excessive water-cures (Naturheilverfahren!), nor to get overdone in any employment. They should avoid *excessive bodily fatigue* in rowing, cycling, &c., and still more in *sexual excess*, as also *the abuse of alcohol and tobacco*. They should not expose themselves to *injuries*, and keep themselves from any strain or overwork of the nervous system, such as are induced by *excessive mental or professional work, or emotion, or great excitement of any kind*. And I may add that it would be well to warn against the use of *hot or steam baths*, which are so frequently used in the treatment of syphilis. One should also remember that

Influenza is a malady which sometimes seems to lead to an outbreak of tabes.

All these warnings, gentlemen, you certainly ought strongly to impress upon your patients, and you should instruct them as to the consequences of any possible folly.

When all this, however, is done, success may not be attained, for people are incredibly careless with regard to future dangers, especially the young, and it will be hard to prevail upon those in the prime of life to adopt a manner of life advisable for the aged so long as the feeling of strength and health is apparently unaffected. At the same time, you may, by such warnings, save many from injurious consequences.

When neurotic patients have had the misfortune to contract syphilis, you will have to make every effort to fight against their nervous debility by means of a well-regulated life, a yearly complete holiday, a spa cure, residence among the mountains, the use of tonics, and also of the bromides in patients of specially irritable constitution. In this connection many a thankful task falls upon the family physician.

II.

In considering the *indicatio causalis*, we naturally meet at once with the exceedingly important question as to *whether in those cases of tabes in which there has been previous syphilis*—which is the case in the great majority of patients —*an anti-syphilitic treatment should be ordered or not.* A rapid glance back to the etiology of tabes shows you at once, gentlemen, that syphilis is indubitably the most important and frequent cause of the disease, and that the time of its development represents the so-called tertiary stage of syphilis; whether it is really a true tertiary manifestation of syphilis is still disputed.

According to the view at present held, the disease is to be considered as a toxic degeneration which arises from the products of tissue change due to the presence in the body of the syphilitic virus (syphilo-toxine). The chronic and progressive character of the disease well indicates that these toxines are constantly present and active, or, at least, that

they are continually freshly produced in batches. They must, therefore, come from somewhere; in some part of the organism—it may be here or there—a focus of disease must exist which contains the disease and produces the toxine that continually invades the blood and lymph.

In any case, this view is more plausible and obvious than that which seeks to do without such a permanent focus of disease, and postulates something set free once, and continuing to act for decades without any fresh impulse.

However one may view the matter, there finally remains the indication to attack the tertiary manifestations of syphilis (which is done in other such-like manifestations more or less easily), or at least to render the probable quiescent foci of disease as far as possible innocuous, so that the further transfer of toxines to the rest of the organism may cease and be prevented. Then experience with other poisons, which induce similar degenerative processes in the nervous system, teaches that the action ceases with the discontinuance of the supply (*e.g.*, alcohol, lead, arsenic, ergot, &c.); indeed, may completely cease and be followed by repair.

We must finally take into account, Gentlemen, that—as fresh facts in increasing number teach—apart from the special changes due to tabes, there are also many others found at the same time which are undoubtedly manifestations of tertiary syphilis (gummatous) in the pia spinalis, the vessels, the substance of the spinal cord itself, possibly also the brain, in which there can be no doubt of the need for, and utility of, an anti-syphilitic treatment.

After these considerations, it cannot well remain doubtful that the question we have asked must be answered in the affirmative: *the use of an anti-syphilitic treatment is indicated for those patients suffering from tabes who were previously syphilitic.* This is the logical result of the views unfolded, which one cannot deny are partly based upon an hypothesis.*

* It stands to reason that in patients who suffer from tabes and have not been syphilitic, no indication for specific treatment is present. I have never said otherwise: nevertheless it has been erroneously stated that I at one time (1879—1881) recommended in every case of tabes an anti-syphilitic treatment, whether lues had preceded it or not; this is completely untrue. I have invariably only spoken of patients suffering from Tabes *who had previously been infected* (by syphilis). That statement, which I believe first cropped up in Naegele's Dissertation (1887), is therefore a pure invention of his or of some other gentleman.

But the justification for carrying out this view in practice can only be based upon the teaching of clinical experience as to whether the result of an anti-syphilitic treatment of tabes is undoubted and satisfactory, or whether, on the other hand, it may not do direct damage and induce the danger of rendering worse an already sufficiently severe disease.

With reference to the first point, I readily admit that up to the present our experience of the utility of anti-syphilitic treatment in tabes has been in no way brilliant, and at all events not very satisfactory.

It is not worth while to go now into all the opinions of different authors on this point in detail.

It is known that the opponents of the view of the connection between syphilis and tabes always use the non-success of the specific treatment as a chief argument in favour of their views. One would naturally not attribute to them any special leaning towards this treatment or any considerable perseverance in the same; but even the adherents of this view have arrived at very similar results, and the most ardent representatives among them have openly confessed their disappointment in the matter. *Fournier*, for example, says that an energetic anti-syphilitic treatment in tabes only leads to isolated real cures, and these only in cases where the disease is combatted in its very earliest stages; also, that it only offers the possibility of limiting and preventing further progress, but not of curing the disease when the latter has gone on for some little time, and that in decided ataxia it is altogether useless; and *Möbius* has repeatedly said that the anti-syphilitic treatment in tabes does not do any good and cannot be of use.

From other quarters, however, more favourable and, in part, even suprisingly good results have been published (by *Rumpf*, *Reumont*, *Schuster*, *O. Berger*, *G. Mayer*, *Landesberg*, *Kowalewsky*, *Fournier* himself, *Dieulafoy*, *Sachs*, *Gittermann*, &c.), and my own results, which now are based upon numerous cases, speak directly in favour of an anti-syphilitic treatment.

If I also can as little report brilliant or certain curative results as others, I have still seen, in many cases, improvement and arrest of the malady; in some, the patients were

so far improved, at least as to their subjective symptoms, their capacity for work and enjoyment of life, that it might be called a very considerable success.

A great part of my own observations have been worked up and published by my colleague, *Dinkler*, and the results obtained are, as far as possible, considering the difficulty of such therapeutic practice, the complicated circumstances, and the usual combination with other therapeutic measures, stated by him in his paper, and may be shortly expressed as follows: that, as far as any injurious effect of the treatment is concerned, there was practically nothing to be said; that *in the greater number of cases a more or less marked and far-reaching improvement in the disease occurred*, and in the others there was neither a positive nor negative effect produced.

Since then I have had collected another whole series of cases, which confirm the above results and have also strengthened my own conviction *that the anti-syphilitic treatment is of decided value in many cases of tabes.* Possibly the way in which this treatment is now carried out, and its being combined with other therapeutic measures, or alternated with them, may have something to do with the result.

I must refrain at this time from giving details in the form of reports of cases. It may be shortly mentioned that I have been able to confirm, through many years, the continued improvement of several cases reported by *Dinkler* (q.v.), and that again I have obtained in a whole series of cases treated by one or more courses of mercury, in conjunction with Nauheim or Rehme, and by tonic after-cures, &c., very considerable improvement: in several cases an improvement almost bordering on cure. For instance, in the case of an officer suffering from recent tabes, he was so far benefited by a single (mercurial) course, that he has, for the past three years, performed his duties as chief of his company without any interruption. The same result occurred in the case of a cavalry officer, who, after one long course of mercury, has continued perfectly fit for his duties during the last two and a half years. I even succeeded in bringing about, by a course of mercury (and galvanism), in quite an old chronic case, such a thorough improvement that the

patient was able once more to take quite long walks without assistance. There is no doubt that these results are very noteworthy. Of course, these cases have to be placed against a number of others where the success was unimportant or wanting altogether.

The other question, *as to whether the specific treatment of tabes may do harm*, and even increase the disease, I can *negative with complete certainty*, basing my opinion on my very extensive experience. It is perfectly incomprehensible to me how many observers can come to the conclusion that the mercurial treatment of tabes does direct damage or may stimulate the disease to more rapid progress.

I have hardly ever seen a careful, well-regulated course of mercury produce any noteworthy injury in tabes; at any rate, not more, or more frequently, than one sees in the treatment by mercury of secondary or tertiary forms of syphilis, or as may occur owing to the intolerance of the drug in a few cases. On the other hand, the patients have nearly always borne the drug well, felt well, and presented a better appearance and increase in weight; on these points conclusive proofs are given in Dinkler's paper, and it is not necessary to lay special weight upon the second case there published. At any rate, *the statement that the mercurial treatment of tabes* (*as also that by iodide of potassium*) *is dangerous and injurious is completely unfounded.*

Notwithstanding these apparently very clear circumstances, one must not ignore all considerations concerning the possibility of a favourable influence over the lesions caused by tabes through a specific treatment. In the first place, it is by no means certain that in this case "*cessante causâ cessat effectus*" holds good—*e.g.*, that with the cessation of the addition of fresh toxine the diseased action is there and then brought to a standstill or even cured; such degenerative processes once set up may continue to slowly advance even if their original cause be removed. Do we not see this in other cases, notably in toxic degeneration and other diseases, where, after the discontinuance of the addition of fresh poison, there is no visible effect on the course of the disease? I will remind you only of the neurotic process and the degeneration of vessels in chronic alcoholism,

or of the continuance of the paralysis and further progress of the chronic interstitial nephritis in lead poisoning, &c. This may also happen in tabes.

Further, it must be remembered that our treatment of tabes first commences at a stage when a large number of the nerve tracts are already attacked by degenerative atrophy and even destroyed; we can hardly reckon on a renewal of these, for do we not know that it is most rare for a real regeneration of degenerated nerve tracts in the central nervous system to take place? indeed, it is said by many to be impossible.

At the best then we can only hope to prevent the progress of the morbid action to the other unaffected nerve tracts, and must leave those already damaged to their fate.

Lastly, when we consider that in a certain number of cases there is also an inherent tendency in the nervous system—either hereditary or sometimes acquired—to progressive chronic degeneration (which perhaps directly determines the localisation of the syphilitic degeneration in certain nerve tracts); when we remember that together with lues there frequently exist also other serious lesions, it will become clear to us that as against such a combination the action of our treatment must be a very limited one.

From the first, then, we dare not raise our expectations too high, and must not be so very much surprised at the frequent uselessness of the anti-syphilitic treatment in tabes which is so often regretted.

This non-success is indeed all too commonly met with in other tertiary affections, and the happy therapeutic illusions which one is apt to nurse and which are based on the brilliant success of the mercurial and iodide treatment of gummatous skin—and throat—affections, and also in the tertiary manifestations, have long since been destroyed by the non-success which very frequently occurs after the most careful treatment of syphilitic disease of the vessels, brain, liver, &c.

After all these considerations concerning the specific treatment of tabes, it appears to me that the following axioms express the conclusions carefully arrived at as to our knowledge of the subject:—*It is in by far the greater number of cases absolutely harmless*; it is in a somewhat large

number of cases *of undoubted use*, and in some cases even *of very considerable value*. In many other cases it is at least *not without some use*, but a certain and not inconsiderable number of cases do remain in which *no visible success occurs*.

The conclusion to be drawn from this appears to me to be perfectly clear: as a rule, *anti-syphilitic treatment is indicated in tabes which has been preceded by syphilis*. But in each individual case this indication is to be severally proved and the treatment dealt out according to the individuality of the patient; under certain conditions also omitting it altogether.

A specific treatment may be recommended with certainty as follows, in:—

1. *All perfectly fresh cases*, on the first appearance of tabes, *in which the primary syphilis did not occur too long ago*.

2. *All cases in which there are still present active symptoms of syphilis*, whether on skin, mucous membrane, bone, &c., or which are complicated perhaps with cerebral or meningeal syphilis.

3. *Those cases in which only an insufficient treatment of syphilis has been carried out*.

In cases where the disease has already far progressed, with well-marked ataxia, or where the employment of long-continued specific courses has already been repeated, you will naturally be more cautious and only decide upon a mercurial course after careful consideration of all the circumstances of the case—*e.g.*, in still progressive disease, in fresh exacerbations if former similar courses (of Hg.) have proved to be useful, &c. In cases where the patient is well nourished you may, on account of the well-known safety of a well-directed mercurial course, wisely venture on a trial of it, but it must be administered freely.

I have even seen cases in which a former specific course had been given without effect which have considerably benefitted by a later mercurial course.

The anti-syphilitic treatment appears to me to be *contra-indicated* in already very old or advanced cases; in very reduced, cachectic, and dyspeptic patients; in those who have already undergone repeated energetic courses without

effect; and lastly, in those patients who show intolerance to mercury and iodide of potassium.

In the *selection of the method of treatment*, we cannot do otherwise than act as in the usual treatment of tertiary forms of syphilis. In the present state of the therapeutics of syphilis it is undoubted that mercurial treatment stands in the forefront, but that, next to it, especially in certain forms, iodide of potassium takes a high place.

The introduction of mercury into the system by means of a well-regulated inunction course appears to me to be the preferable mode. I know, of course, that one may employ internal administration or subcutaneous injections, or make use of the combinations of mercury which are not easily soluble (Schwerlöslich). But the dangers which the latter incur have already called forth a general mistrust of them, so that they may be left out of account. With regard to internal administration, I have frequently met with disturbances of the digestion and general nutrition, together with insufficient action, and in the subcutaneous injections of the sublimate I have repeatedly found that they remain without any action, notwithstanding long energetic use by others, whereas afterwards a course of inunctions was successful; therefore, I have seen no reason to employ them.

I almost invariably use the method of inunction, in moderate doses (4-6 grm. ung. ciner. daily), with all precautions; very careful treatment of the mouth, baths of 26° to 27° R., very good nourishment, and plenty of fresh air.* This is thoroughly well tolerated by almost all patients; they look better, increase in weight, and stomatitis or diarrhœa hardly ever occur. I order 30 or 40, even 50 or 60, such inunctions one after another, according to the circumstances and individuality of the case.

Then, under all circumstances, a *pause* follows, which may be longer or shorter (4 to 12 months), and this pause I now occupy, as a rule, *with general tonic treatment*—mountain air, a short spa cure, especially sitz baths of 24-18° R., and the internal administration of tonic pills (ferri lact.,

* Whether at the same time the drinking of sulphur water or other water of a like kind is useful, as recommended by Reumont and Mayer (Aachen), I must leave an open question; the Aix-la-Chapelle experiences are in favour of it.

ext. chin. aqu., ext. nux vom., &c.), electrical treatment, and eventually perhaps a spa cure at Nauheim or Rehme. This appears to me to be of special importance, and you will usually see the first signs of benefit during this after-cure subsequent to the mercurial course. This is, indeed, quite self-evident according to the idea we have of the method of action of the mercury. It should remove the causative disease products, and thereby prevent the further progress of the disease and render more easy and possible the regeneration of the damaged nerve tracts. The mercurial course really only prepares the soil for the better and more certain action of the other therapeutic procedures with which we directly attack the disease. It is then in no way a specific against tabes itself, but only against its cause.

And therefore, gentlemen, you must neither expect yourself nor lead your patients to expect a remarkably direct benefit *during* the mercurial course, or disappointments will result. But you must be prepared for the chief improvement to occur *subsequently*; this is most important.

Not infrequently, I *combine a spa cure with the mercurial course;* that this can be carried out at Aix-la-Chapelle in a very specially suitable way is known. You must only warn the tabes patients that very hot baths are preferably given there, and they must not go higher than 26 to 27° R.

I also combine the mercurial course with the baths of Rehme and Nauheim, which combination is also, as a rule, excellently borne. Of course, you can make the combination also at Wiesbaden or Baden-Baden, at Baden in Aargau, or Baden near Vienna, at Nenndorf, or at other sulphur spas; at various saline baths, also very satisfactorily in well-ordered nervous sanatory establishments, in hospitals and sanatoria, and eventually other methods of cure may also be combined, such as the Faradic brush, galvanism, hydrotherapeutics, gymnastics, suspension, &c., which will be mentioned later on.

On the other hand, *such an inunction course should not be tried on patients going about their usual employments; this must be distinctly warned against.* Under these circumstances, it is, as a rule, badly borne, of no possible use, and is only capable of discrediting the method of treatment.

As to when and how often this "cure" is to be repeated, it is impossible to lay down general rules. It will quite depend upon the individual case, on the effects produced, on the progress of the disease, and on possible exacerbations.

In general, you must not expect that a single course will be sufficient; several will be required, and what syphilographers understand by a "good mercurial course" will be needed—viz., repeated alternate severe and mild courses, separated by sufficiently long intervals (*Neisser*). I do not, as a rule, permit them in shorter intervals than six to nine months; several of my patients go through such a (mercurial) course every year or every two years (25 to 30 inunctions), and they are quite contented with this; but, of course, the cases vary very much.

The treatment of tabes by iodide of potassium has, for a long time, had its advocates; it does not appear to me to have such evident effect as quicksilver. Naturally, however, trials with this drug are also proper and advisable, and may be of especial use in cases where there are specific meningeal and vascular complications. It may be tried between the mercurial courses, before or after the tonic treatment, which I mentioned above, or even used for a long time independently by itself—*e.g.*, for one to three months in the usual doses—1·5 to 4·0 grm. and over daily, in alkaline water or milk. It appears to me to be specially indicated in cases complicated by tertiary syphilitic affections of the skin, the mucous membrane or bones, with cerebral syphilis; also in cases with severe lancinating pains, with rapidly-progressing symptoms, with peripheral neuritis, &c.

The last word has not been said as to whether the treatment of these late forms and sequelæ of syphilis, with mercury and iodide of potassium, is the most correct and successful; possibly other means and other methods of application might lead to better results; they are, however, still to be found. A few attempts that I made in severe cases with Zittmann's cure, with Rood Laffecteur, and such-like, have not satisfied me.

Possibly the future may teach us better; the anti-toxine may possibly have to be considered. In any case, it is to be wished, on account of the numbers of unfortunate patients

attacked by the disease, that a more certain method than we yet have may be discovered, whereby we may treat these late manifestations of syphilis, especially of the central nervous system.

It is seldom possible to carry out any other "causal" indications in tabes. The cause of the disease is so distant in the past, and so impossible to undo, that only in rare cases is it possible to get rid of the still-existing and still-working mischief; so one has to urge upon patients to give up the bad conditions in which they are living—such as continual exposure to cold and fatigue, living in damp workshops, offices and bedrooms, indulging in excess either sexual or of alcohol or tobacco, or bearing too great mental strain or emotional excitement. But generally, gentlemen, that is all there is—except syphilis—upon which to direct your fundamental therapeutic measures.

III.

Now that I turn to the fulfilment of the *indicatio morbi*—*i.e.*, to the treatment of the disease of tabes itself—it may be said that the specific treatment has already been given in my previous remarks; but this would only be in so far correct if we, without hesitation, hold tabes to be a form of tertiary syphilis, and not a disease following it. You know that to this hour this is only an hypothesis. You know, further, gentlemen, that specific treatment has had very unsatisfactory results in many cases, and lastly, that there is a very small group of cases of tabes in which no history of previous syphilis has been proved. There remains, then, a wide field for the *direct treatment of tabes*, either *without any specific treatment or together with it.*

But having accomplished the *indicatio causalis*, we have still the duty of fighting and curing the disease itself—in other words, we have to adjust and to remove the grey degeneration of the posterior column of the spinal cord, and in many peripheral nerves, &c., or, possibly better expressed from the clinical standpoint, we have *to adjust the functional disturbances which are present*, so that the patient may be again fully capable of work and feel himself free from all debility.

This is, indeed, the chief end—practically the only thing worth striving after. Theoretically, it may be demanded that we should obtain a "pathological cure"—*i.e.*, the disappearance of the grey degeneration from the nerve tracts; practically, however, it is quite sufficient if the functional disturbances are reduced to an inappreciable remainder, and the patients are again fully capable of work. It will be perfectly immaterial to them whether they continue to have a grey degeneration left, or if even a few symptoms still remain, as, for instance, the abolition of the pupil reflex to light, or the absence of tendon reflexes, which cause no manner of inconvenience to the patient.

A great number of means may be adopted to reach the goal, all of which have been recommended with great insistence—drugs, baths, hydro-therapeutics, all kinds of physical and mechanical procedures, electricity, massage, gymnastics, various surgical and orthopædic operations, the administration of extracts, psycho-therapeutics, &c.

If one views these methods and their results without prejudice, one has unfortunately to come to the conclusion that none of them have rendered exceptional service, and that there can be no expectation of any of them yielding definite results. It is always only a small number of cases in which favourable results are attained by any of them. In the majority of cases they fail, and even the isolated cases are very varied in the way they react to single methods employed —sometimes only one method, sometimes another being successful. It is seldom that one can say beforehand with any approach to certainty that this or that treatment will be beneficial in a given case, and so our treatment of tabes remains always a matter more or less of experiment, a search for the proper method.

Try to picture to yourself an idea of the way in which Nature could produce an adjustment or cure of the original lesion in tabes, and you will have to admit that the disease probably has to do with a poisonous action (endogenous or exogenous), a disturbance of the nutrition in the nerve elements (the neuroma), which, commencing in alterations in the chemical action, leads to a true visible degeneration. Nature adjusts such lesions usually by means of an increased

and better metabolism, at the same time stimulating and raising the circulation of the blood, and probably also by elimination of the toxic elements. These purposes are best served by a *general increase in nourishment*, by *stimulating the whole of the metabolic processes*, and *thereby altering the chemical action in the diseased nerve tracts, on the one hand, and, on the other, mildly stimulating the functions of similar* (dergleichen) *nerve tracts, while rendering at the same time their blood supply easier.* Looked at from this standpoint, we shall rightly consider the following methods as the best to employ.

Their number and variety is very great, and therefore a concise account of the treatment of tabes is hardly possible. Let me, then, present to you, in the first place, the several means and methods (of treatment) in order, together with remarks on one's experience concerning them.

Before this, however, permit me, gentlemen, to give you some advice as to the *general dietary and mode of life* for sufferers from tabes. My remarks will apply to the great majority of such patients, certainly in the later stages of the disease, but they deserve to be followed in the early stages as well; indeed, in the very earliest.

To these patients, mostly men in their prime, full of life and activity, little likely to care for their bodies, I am in the habit of saying, "Live sensibly, as if you were an old man; be quiet and regular, avoiding all exertion and fatigue of every kind, shunning every excess and emotion: that is the best for you."

As a matter of fact, you can give these patients no better advice. They must be temperate in eating and drinking, should partake of simple, non-stimulating, but at the same time nourishing mixed diet, avoid as far as possible all excitement; drink and smoke very little; in all work they should be very moderate, have the necessary intervals of repose, and plenty of sleep. They should seek simple amusements and recreations, but strictly avoid every exciting and tiring company and anything emotional, such as gambling, business speculations, political debates, &c. In sexual matters they should be extremely moderate, avoiding all undue sexual excitement. (You may, however, permit many

patients in the first stages of the disease moderate sexual intercourse.) They should have as much fresh air, and be out as much as possible, using a bath chair if needful, and each summer should take a change of air, choosing, by preference, for their residence, a place where there is forest or mountain air, on account of its action on the appetite, on tissue change, nutrition, and the formation of blood. In winter they may pass the time in the South (Meran, Arco, Abbazia, the Riviera, or South Italy, &c.) in order to enjoy the fresh air, light, and sunshine to the full. Finally, they must be extremely cautious in respect to bodily exertion and fatigue. This last point is one of the most difficult, and requires careful and exact attention in each individual case.

In general, I am in the habit of impressing every tabic patient with the fact that before all things they should avoid all over-exertion and fatigue and especially such exertion as hunting, mountaineering, or any kind of sport. But apart from this, it is advisable to give certain hints with regard to simple fatigue: they should only continue exercise until they *begin* to feel tired and then rest: should remember before every walk that the return has to be accomplished, and, with these precautions, all kinds of exercise, gymnastics, rowing and even moderate horse exercise may be permitted.

In some cases it is very difficult indeed to say how far one dare go in the particular stage of the disease. In early and still progressing cases it appears to me that the greatest caution is necessary, whereas in older cases, which have become more stationary, with well-marked ataxia, greater weight is to be laid upon regular muscular exercise, movement and gymnastics, as you will hear later on.

With reference to the theory recently developed by *Edinger** from a new and interesting point of view, the question occurs whether complete rest of body, a long confinement to bed, especially at the commencement of the disease, is not to be advised. Much may be said for it, and it is perfectly certain to be recommended in the suddenly-developed and rapidly-progressing forms, for those, for instance, in-

* L. Edinger, Eine neue Theorie uber die Ursachen einige Nervenkrankheiten, insbesondere der Neuritis und der Tabes. Samml. Klin. Vortr. Neue Folge, No. 106, 1894.

duecd by bodily or sexual over-exertion, whieh very rapidly develop ataxia; more detailed experiments arc to be desired in this connection. These regulations can hardly be earried out or expected of the patient in the very chronic ordinary forms of tabes, and in chronic far-devcloped cases; for these we should rather, as beforc mentioned, advise the opposite trcatment—movement and muscular exercises.

Turning now to the discussion of certain means and plans of treatment, it may be said, *of drugs* at least, that, much as they are still used, and essential as they are in the long duration of the disease, it is very difficult to arrive at a certain opinion in regard to their action, as nope of them sccm to produce a prompt or brilliant cffect, and as other methods are usually cmployed at the same time.

Nitrate of silver may still be most depended upon, and is apparently useful in a seetion of the cases literature furnishes us with. There would seem to be also some eases of undoubted cure or, at any rate, of almost eomplete cure and of long duration. This remedy must, however, be given for a long time—for months, with considerable intervals. It is best administered in pills, 3 to 5 cg. a day, judieiously eombined with ext. nue. vom. spir., so that during the eourse of two to four ycars at least 8 or 12 grm. of the drug will bc used, sometimes even more.

Ergot has been mueh recommended and extensively used, cspeeially by *Charcot* (0.20 pro dosi., two to three times a day for some weeks, and then an interval), but I have never seen any real success with it, and have been very cautious in its administration cver since *Tuczek's* work, "Ergot in Tabes." Still, it docs seem to have a eertain chemical affinity for the posterior column of the spinal cord, and the possibility of its beneficial aetion in small doses is not to be put aside without further experience.

Arsenic is espccially and forcibly advised by English authors (*Gowers*, *Byrom-Bramwell*, and others). I have not yet succeeded in making sure that this drug, so wonderfully powerful in many directions (think only of chorea minor, severe anæmia, pseudo-leukœmia, neuralgias, malarial cachexia, psoriasis, Liehen ruber!), achieves dcfinite rcsults also in tabes. Possibly it only acts as a tonic and hæmos-

tatic, but possibly also as a nerve tonic (nervinum), and, in any case, it deserves more frequent use in the regular preparations (such as Fowler's solution, Levico water, and subcutaneous injections).

Iodide of potassium is lauded by many, partly as a purely curative agent, partly as a chief agent against the lancinating pains. Those who consider tabes as a disease induced by syphilis will not find this wonderful. I have already said all that is needful on this subject. Besides, iodide of potassium is a drug possessing such many-sided properties that it is worth while trying again and again (doses, 1 to 4 grm. daily in a weak solution with some bicarbonate of soda).

Of the *bromide salts* there is less to say, although these drugs have found ready advocates for their use in tabes, and not *only* as a calming, symptomatic agent. I have never seen any special use in them.

I have recently gone back, with I consider good results, to a drug which was formerly widely recommended, then prohibited and quite forgotten—namely, *strychnine*. How it acts is indeed hard to say; whether it especially affects definite parts of the spinal cord and definite changes in the nerve tracts is open to question; possibly it has only a general tonic action as a stomachic and nerve tonic. But that it acts, and not infrequently acts favourably, appears to me indubitable, apart from its special action on pallor and the sexual apparatus; and this confirms *Naunyn's* experience of strychnine injections in severe myelitis with spastic symptoms. I apply the drug either in the form of subcutaneous injections (each containing 2, 4, 8, or 10 mg.), or in the form of the tincture, or the alcoholic extract of nux vomica, preferably in combination with other drugs—with arsenic, nitrate of silver, with Vin Condurango, and especially often with the "proper tonics."

And this leads me to say a good word for these latter. It is not improbable—after the line of thought already sketched—that tonics (I have in my mind only preparations of iron and quinine and possibly also arsenic) may have a favourable influence upon the disease of tabes, that at any rate they are likely to at least aid the natural powers of the organism towards recovery. It is not necessary in this connection to

infer a specific action upon the process of disease, although indeed this might also be possible. Who knows with sufficient accuracy the minuter chemical changes in the diseases of the nervous system, or the complicated chemical combinations of the dormant molecular powers of the organic drugs, to venture a decision on the point?

Many years ago (due to some literary stimulus) I drew up a formula for a compound pill containing iron, extract of bark, and nux vomica.* It is entered at my clinic by the name of "Pilulæ tonicæ." These pills are exceptionally well tolerated, and I have proved their value in innumerable cases of anæmia, neurasthenia, hysteria, &c., and more recently in many cases of tabes. When used in this last disease, after they have been tried alternately with nitrate of silver, ergot, &c., I have often heard the wish expressed by patients to have the tonic pills again; I have already referred to them in speaking of the after-cure subsequent to mercurial courses, and believe that they have in many cases an exceptionally favourable action upon the general condition, disposition, and spirits of the patient, and at the same time upon the symptoms of tabes. In any case, they deserve a high place in the therapeutic treatment of tabes.

Of all the other drugs recommended in tabes—gold and sodium chloride, barium chloride, quinine, antipyrine, phosphorus, &c.—it is better to be silent; no certain results are known from any of them.

On the other hand, a few words must be said concerning the recent use of *organic extracts* in treatment. After the astonishing statements of *Brown-Séquard* on the action of orchitic fluid; after the statements of *Poehl* concerning spermin, which are not without a scientific background; after the injections of sheep's brain extract by *Const. Paul* brought forward with some amount of certainty; and lastly after the really astounding action of thyroid preparations in myxodema, cachexia thyreopriva, goitre, and obesity, the

* R. Ferr. lactic., 3·0—5·0.
Extr. chin. aqu., 4·0—5·0.
Extr. nuc. vom. spir., 0·4—0·8.
Extr. gentian., q.s.—Pilul 100.
Sig.—One or two pills thrice daily after food. The dose of the various ingredients to be modified by the individual case and any special indications.

possible employment of such things in tabes is not to be straightway denied; have we not here to do in the first place with chemical changes? And so a whole host of unfortunate patients suffering from tabes joyfully demanded this treatment, which was administered by credulous doctors with some reputed success. In the end, however, not much has been gained; unfortunate complications occurred, and the matter is again in abeyance. I have only made a few trials myself with "Brown-Séquardine" and with spermin, and reserve a definite opinion, but should not like to dissuade from further trials.

The same may be said for the recently-introduced subcutaneous and internal use of the *glycero-phosphoric acids* and their salts, which are said to act as nerve tonics, but which have not yet had a sufficient trial.

In the consideration of the treatment of tabes, the important *rôle* which *baths and spa cures* play I may briefly dismiss, as I have not much to add to what I said 20 years ago in my handbook on the diseases of the spinal cord. My subsequent very extensive experience has only confirmed in the main the views then expressed.

Let me, then, pass over in a few words the action of the various baths. We know little definite about it; we can only imagine that they are able to modify, in a favourable manner, the tabic process, by the temperature of the baths, their saline and carbonic acid constituents, their action upon the skin, upon the circulation and respiration, as well as upon general metabolism and nutrition, and their special action upon the nervous system, sleep, stimulation of the functions, especially of the centripetal nerve tracts, &c.; more we do not know.

To-day I must place in the first rank with greater certainty than formerly the *thermal salt baths*, containing CO_2 *Nauheim* and *Rehme*. In most cases they have a favourable, stimulating and refreshing action upon tabic patients, many hundreds of whom collect yearly at these spas, and the fact that many of these patients return many times, year after year, to the baths speaks for their favourable action. The spa physicians there are accurately acquainted with the kinds of baths most beneficial to cases of tabes, and therefore the

patients have the best chance of gaining good. The temperature, amount of gas, and kind of bath water (shower, douche, &c.) can be modified at will, and according to the indications of the case; it is best to leave all that to the spa physician. As a rule, medium and low temperatures are indicated, a moderate amount of CO_2, and moderate movement in the water. This suits nearly all patients with tabes, at any rate those with very irritable nervous systems, with violent attacks of pain, and with thermohyperæsthesia of the skin of the trunk.

The *iron baths*, rich in CO_2, and some also in salt (Schwalbach, the Kniebis baths, Cudowa, Franzensbad, Tarasp-Schuls, St. Moritz, &c.), act quite similarly, even identically, and they must be ordered and applied according to the same rules, and are possibly to be preferred when one wishes to combine the blood-forming and tonic action of the iron baths with mountain air. Concerning the action of mud baths, for which formerly some good success was claimed, we have lately heard less of them; indications for their use are difficult to state with precision.

My recent experiences give me no cause to modify my former less favourable opinion of the *indifferent hot springs* (Schlangenbad, Wildbad, Ragaz, Gastein, Teplitz, &c.; also Baden-Baden and Wiesbaden). I am still convinced that the indifferent warm baths, especially those of high temperature, are really injurious for most patients suffering from tabes; still, even now I meet with many a patient who has been ordered there by others and suffered harm. On the other hand, there are isolated cases, especially those of a very erethic and irritable character, with hyperæsthesias, severe pains, crises, &c., in which they are of use, so that now and then they may be tried. At the same time, the rule must be strictly observed that the temperature must not be above 26 to 27° R. (32 to 33° C.), that the baths must only last for 8 to 10 minutes, and only be given three or four times a week.

Sulphur baths (Aachen, Nenndorf, Baden i/A, Baden b/W, the Pyrenese baths, &c.), so widely recommended, probably claim in tabes no other action than the indifferent waters, and should therefore be ordered with the same precautions

as those. If they are tried, owing to their anti-syphilitic action, it is most necessary to warn against the high temperatures, so much liked in the treatment of syphilis.

Lamalou (a weak, warm, iron spa), recently almost exclusively advised by the French School for tabes, appears, according to the information I have obtained, to have no advantages whatever over other hot springs.

After what I have repeatedly said, it is hardly needful to warn all patients suffering from tabes *against hot steam or air baths.*

It seems to me that almost greater weight must be laid on *Hydrotherapeutics* (the water cure) than on *Balneotherapeutics* in the treatment of tabes. In hundreds of cases of tabes which I have observed, the success of this treatment has been very marked; this may be fully explained by the undoubted action of a water cure upon tissue change, nutrition and body weight, upon the energy of the cutaneous functions and the ensuing hardening, upon the general *schablonenhaften*, and most ignorantly directed application by the stimulation of the sensory neuroma, which is primarily attacked in tabes, and lastly through stimulation of the functions of circulation and nutrition in the central nervous system. Naturally all depends on the methods employed, and on their proper use in individual cases. In general, all procedures which act strongly, which excite or cause a sudden shock, should be warned against; also perfectly cold baths, douches, massage, wet packing, shower baths, &c., and, of course, all "cures" such as at Wörishofen and its branches, so sought after by many invalids. I have seen not a few patients who have been greatly harmed by the usual *schablonenhaften*, and most ignorantly directed application of water, though certainly a few who managed to stand it experienced some benefit in their general condition. But under all circumstances, mild, careful, and long-continued methods are to be greatly preferred. In the first place, *sitz baths*, of a medium temperature (24 to 16° R.), of short duration (5 to 2 minutes), then simple *wet rubbing*, *tepid baths* (25 to 24° R.), *local spinal* and *foot washings*, &c., employed according to the modern principles of hydrotherapeutics. The chief point is naturally the choice of a health

establishment, which should by preference be situated in a forest or hilly region, and to ensure that the treatment be carried out by a physician who possesses the necessary special knowledge and caution, and who will exercise great care in the treatment. Nearly all patients suffering from tabes may be treated on the above lines, adapted, of course, to the individual requirements. There are only a very few who cannot undergo this treatment, and these are patients, as a rule, who are much run down, irritable, anæmic, and with degenerated blood vessels and vasomotor symptoms. *Tepid foot baths* may be advantageously used by many patients in summer, with the precautions already mentioned. On the other hand, sea baths, especially with a very low temperature (10 to 13° R.) and rough seas, are, as a rule, contra-indicated. Incautious bathing, especially at northern sea-side places, may easily render patients worse, yet I do remember a few cases in which a very cautious use of sea-bathing (in a calm sea, a high temperature, and for 1 to 1½ minute every two or three days) was of distinct benefit.

Again, the very thorough investigations of *R. Remak* in *electrotherapeutics* are of outstanding importance in regard to tabes. But the remarks which I have already made as to therapeutic measures for tabes in general apply here too; only in a few cases does this method give us brilliant success, though in many cases we at least find improvement and alleviation, and even arrest of the malady; in many others it leaves us in the lurch. That cannot, however, be helped, and should not prevent us from making use of this powerful physical treatment again and again. The tendency which has recently become customary to discredit electro-therapeutics, by regarding their action chiefly as "a suggestion," appears to me—in the face of numerous undoubted successes—to be wholly unjustifiable in respect to tabes, and I should be sorry to be without electricity as one of the possible methods of treatment of the disease. But it is of the greatest importance to insist upon its being applied with technical skill, consistency, and in the right way, as otherwise it is apt to do more harm than good. Nowadays there is far too much electrifying by the laity, and even by physicians, who understand nothing about the matter, who electrify with

unsuitable electrodes and currents, with improper physical and physiological points of application, without rule or consistency, and who, by the belief that possible success depends only upon suggestion, are strengthened in these bad habits, and so this very beneficial means is discredited. I cannot too strongly request you, Gentlemen, to take these remarks to heart, and if you wish to use electricity, either to give its application careful study yourselves or to hand the matter over to a specialist.

This is not the place to go into further detail as to the manner in which electricity acts; indeed, I have nothing to say about it which has not already been said by myself and others; the action here also is upon the processes of nutrition, upon the circulation, and upon the diseased portion of the spinal cord and nerves; it may be effected in various ways.

The most certain and adaptable way is with the *galvanic current*; you can study the special methods in the text-books on electro-therapeutics; all I can do here is to throw out a few hints. In this disease, along the spinal cord, application of the current in the same direction is quite right—one pole at the neck, the other in the lumbar region, the current passing up or down, both the electrodes fixed or the upper one being moved slowly up and down: in other words, covering various points. Or the method of galvanisation of the sympathetic at the same time may be used (kathode over the sympathetic in the neck, anode at varying points along the spine, from the first dorsal vertebra to the first lumbar, continued for one or two minutes at each position; then, the anode being still below, the kathode above is moved slowly up and down). But you may pass the current through the body too, placing the indifferent electrode upon the sternum or epigastrium, and the other electrode on the back successively on various points, until you have treated the whole of the affected parts. In early cases with symptoms of irritation, the anode should be used, in older cases the kathode on the back, or both may be used, one after the other, it is questionable whether this much matters.

This polar treatment of the back, especially with the anode, may also be used with advantage in sensitiveness of single

spinal processes, in girdle pains, intercostal neuralgia, and the girdle-like hyperæsthesia found on the trunk in tabes. I generally add to the treatment of the spinal cord the peripheral treatment of the legs (anode upon the lumbar enlargement, kathode upwards along the course of the crural and ischiatic nerves).

It must be specially noted that large electrodes should be used for the back (oval, 50 to 70 qcm), that they are to be thoroughly wet, properly applied and directed (*geführt*). All this needs to be practically learnt—moderate currents, not too long sittings.

I have largely employed these methods up to the present time, and do not doubt that they have often been of use, sometimes more, sometimes less, both for the general disease as also for symptoms; but of the treatment of symptoms more anon.

One uses the *Faradic current* in tabes—apart from treating symptoms—much less frequently than the galvanic. Only *one* method of application, since it was advised by Rumpf, has maintained a certain prominence, and that is the Faradic brushing of the skin of the body and extremities with a fairly strong current for 5 to 20 minutes daily, so that definite feeling, if not considerable pain, results.

It is quite conceivable that this stimulation of the functions of the specially diseased sensitive nerves may have a favourable influence upon their regeneration. Rumpf obtained especially good results when this treatment was combined with mercurial inunctions. Cases with well-marked anæsthesia of the back and legs, with lancinating pains, seem most particularly suited to this treatment. I have also frequently seen it used with advantage.

I have no experience of the employment of *static electricity* in tabes, and have none to report of other observers.

I still have to mention another method of treatment, once much in vogue, then put aside, but now again more practised —namely, *revulsion to the skin*.

In former times very much mischief was done thereby; the whole back was scored with red-hot irons and moxas; now one makes use of the very much milder and nearly universal method of Paqueline's cautery, especially in the

form of *Pointes de feu*, used chiefly by *Charcot* and his school, who employ it very largely and possibly even rather to excess. Apart from this, the same end may be attained by applying flying blisters or iodine paint along the spinal column or by means of rubefacient liniments and plasters.

The *Pointes de feu* are best applied with a small thermo-cautery on 30 to 50 points, covering an area the size of the palm of a small hand, alternately on either side along the spinal column, once every eight or ten days; the procedure may be continued for months. In a similar way, you may employ the flying blisters or iodine paint daily over larger or smaller areas of the spinal column, according to the sensitiveness of the skin. Various strengths of tincture of iodine may be used (according to *Erlenmeyer*, pure iodine with iodide of potassium may be used, or the iodine may be mitigated by the addition of tinct. Gallar) until the skin is so sore that a few days' rest must be given.

I have employed these methods recently very frequently, especially in cases accompanied by pain in the back, girdle sensations, severe pain, gastric crises, &c., without being struck by any very evident action; still, I have repeatedly seen good results follow, therefore I can recommend these methods for occasional employment; the long duration of the malady gives full opportunity for their use amongst others.

During the last 20 years a series of chirurgical orthopædical methods of treatment have been brought forward. Some have aroused great attention, and called forth a certain enthusiasm, but they are already, to some extent, threatened with oblivion; possibly this it not quite justifiable, for one certainly sees in isolated cases these methods producing indubitable and sometimes even astonishing results.

As the simplest and least wonderful of these methods, I may first mention *massage* and *gymnastics*. The first can obviously be useful in certain directions, by stimulating the circulation in the skin and the muscles (and at the same time possibly also in the deeper parts), by increasing tissue and general nutrition, the strength of muscular power, and overcoming ataxia and paresis, and lastly, probably also by stimulating the sensitive nerve tracts and inciting the functions and tissue change in the peripheral nerves.

I have seen a large number of cases in which *massage* (after various methods, German and Swedish) has been very well borne by the patients and used with decided benefit. Badly nourished, emaciated individuals, with flabby muscles, weak digestion, well-marked disorders of sensation and commencing ataxia, are especially fitted for this treatment. I shall refer later to the use of massage in overcoming special symptoms.

Gymnastics naturally act in a somewhat similar way—partly as a general means of invigoration, heightening muscular nutrition and the power and certainty of muscular action, and at the same time eventually acting favourably upon the disease of the spinal cord itself. The chief field, however, for the use of gymnastics is to be found in overcoming the ataxia, of which I shall speak later. It has developed recently into quite a successful and active method. As a matter of course, gymnastics should be principally tried in patients who are still robust and muscular.

I mention, not without some hesitation, *nerve-stretching*, which for a long time was very much discussed but now has almost vanished from the scene. Without doubt the "bloody nerve-stretching" has now almost no advocates, and the more recently substituted "bloodless stretching" very few.

Commencing with the success of nerve-stretching in severe neuralgias, especially in sciatica, the procedure was first tried in tabes dolorosa. Certainly at first some few noteworthy results were obtained, and a definite method of treatment was formulated (Langenbuch). One did not even refrain from thoroughly stretching both the ischiatic nerves and both the crural nerves, sometimes at one sitting, until the dangers which ensued, in consequence of the operation, together with some deaths, as well as many failures, cooled the ardour considerably.

Even if it appeared to be *à priori* completely incomprehensible how tearing and stretching of single nerves, even if they extended to the roots and the meninges, could favourably influence the process of grey degeneration in the whole of the spinal cord, this would be no hindrance, if only the results were to some extent constant or to any extent re-

markable; but do our newest views concerning the real seat of the anatomical lesions in tabes—in the posterior root area, in the sensitive Neuron I., possibly in the spinal ganglions—bring any nearer the *possibility* of an influence by forcible stretching on the peripheral nerves?

But these successes, so startling and considerable as they may have been in isolated cases, are certainly not such as to justify the undertaking of severe surgical measures in the common run of cases, and if the enthusiastic and even now still firm upholder of nerve stretching, *Benedict*, has given expression to the conviction that "possibly even in the next generation not operating at the commencement of tabes will be viewed as a scientific mistake," certainly the present generation does not feel its conscience in any way burdened by this sin of omission.

At most, it is in those rare cases of very intractable neuralgias of tabes, almost localised in definite nerves with real "ischiatic" crises, that an indication for a "sanguineous nerve stretching" can be justified, all the more as it may be done under strict antiseptic precautions with hardly any risk.

And in these cases, gentlemen, you will be able to do as much good with the more recently-practised *bloodless nerve-stretching*, according to various methods, without risking the patient's life. The method was, I think, first recommended by *v. Corral*, in which the outstretched legs of the patient, lying upon his back, are so bent over at the hips that the feet are brought to either side of the head, and held in this position for some time. Similar is the method recommended by Hegar of "stretching the spinal cord": the head and chest of the patient, sitting upon a firm table with outstretched lower extremities, are forcibly bent down forwards. *Bonuzzi's* method is still more energetic; it is much praised by *Benedict*. It consists in this: that the legs of a patient, lying on his back, with his head supported, are seized with a towel at the ankles, and are then pulled so energetically over the head that, with forcible bending forward of the spinal column, the knees are brought as far as the forehead, even being pushed on each side of the head downwards with force. The procedure is very painful, and

not at all without danger, as it may produce all kinds of disastrous consequences. Lastly, *Blondell's* method is much less severe: he places the bent knees of the patient as near as possible to the chin, and keeps them there for five minutes daily, aided by a bandage placed round the neck and underneath the knees.

All these methods are credited with good results, especially for lancinating pains; they probably act, not only by stretching the nerves (especially the ischiatics, to which most attention is paid), but probably still more the spinal column, which is stretched in its posterior half; a loosening of the peripheral nerve, also of the spinal ganglions, possibly also a stretching of the posterior roots, may be attained by this method.

On the effect of this method upon the spinal column depends finally a still further method of treating tabes, which has been introduced quite recently—namely, *suspension*. First made known by *Motschutkowsky's* report of striking results in 1883, it found later earnest supporters in *Charcot* and his school, and was then tried and studied everywhere with great zeal. *Worotynski* has quite recently given a detailed, succinct description of it.*

It consists in this: that the patient is suspended by the chin and neck, and at the same time by bands under the arms, in a *Sayre's* suspension apparatus, and kept in this position for 1, 2, or 5 minutes once a day or every two or three days. In this case the full weight of the body acts as a stretching weight, the vertebral column is lengthened, and probably also a pull is given to the meninges and nerve roots.

Less severe, and probably also more convenient, is the treatment with *Sprimon's* suspension apparatus, in which the patient, in a sitting position, is fastened at the elbows, as well as at the chin and neck, and by means of a weight led over a pulley, which one can vary at will (50, 100, or 150 lbs.), is raised up. This method is capable of much more accurate gradation, and is not liable to the dangers incurred by the former method, in which grave symptoms

* Worotynski, Ueber die Suspension als eine Behandlungsmethode bei Nervenkrankheiten. Deutsch. Zeitschr. f. Nervenheilk., Bd. VIII., S. 75, 1896.

and even death have been observed. It can therefore be applied more frequently and for a longer time, even up to 10 or 20 minutes a day, or even several times a day.

Other still milder procedures exist (*Bogrow*, *McLane*, *Hamilton*, *M. Weiss*, and others) in which the patient has the head or the shoulders fixed when lying upon a more or less steep slope, and the stretching force is left to the weight of the body; similar to what is frequently used by surgeons in extension of the spinal column.

Many endeavours have been made to find a plausible explanation for the undoubtedly favourable action of this procedure—also by experiments on the cadaver and on animals—but up to now with little success; one after another the following explanations have been considered: the freeing of the spinal column, the widening of the inter-vertebral notches and vertebræ, the freer circulation in the nerve roots and spinal ganglia, the stretching of the membranes, the roots, and the spinal cord itself, the breaking down of meningeal adhesions and the softening of indurated neuroglia; also the influence upon the medulla and the brain, &c.; but I will not weary you with a discussion upon these various views.

In any case, so much is certain, that by means of suspension a whole series of successes has been obtained, and sometimes very considerable success, in tabes, as well in respect of the whole progress of the disease as in regard to isolated symptoms, such as lancinating pains, girdle and cuirass sensations, anæsthesia, alteration in muscular sense, ataxia, vesical weakness, impotence, &c.; even atrophy of the ocular nerves is said to have been improved by this treatment. The number and reality of these successes is too great for them to be simply denied, nor can they be dismissed by the favourite explanation of "suggestion." What a blessing it would be if one could treat tabes merely by suggestion! We have, however, not yet heard that the most active suggestion in hypnosis has had any particularly brilliant result in tabes.

I have myself seen a series of favourable successes from suspension, and I still frequently employ it. One must, however, not hide the fact that many failures are to be

recorded, and that suspension, especially according to the original method, is not without danger. A very heavy patient, or advanced age, disease of the heart or vessels, and brain disturbance are contra-indications which must be especially noted, but it is more difficult to lay down exact indications for suspension. It appears to me that emaciated individuals, cases with lancinating pains, with gastric crises, with bladder and sexual weakness, with girdle and cuirass sensations, with commencing ataxia, &c., are especially suited to this treatment, which can be combined with many other therapeutic methods.

It is convenient to mention in this place that still another method has been brought forward which seeks to supply a permanent moderate extension of the spinal cord, by means of *a mechanical support and relief to the spinal column*, in the form of a well-fitting, substantial *corset*. First introduced by the orthopædic surgeon, *Hessing*, and enthusiastically recommended by *Jürgensen*, this method, in combination with a very long-continued treatment in a hospital, together with very good nourishment, gives many patients considerable ease; they should first lose their bladder troubles, then the pains and paræsthesia: gradually the power of walking should become better, and in some cases even cure take place. Too much credit, however, is not to be given to this treatment, and in many cases the enormous cost of such a corset yields very little profit. As a matter of fact, they can now be procured at other places besides Göppingen, in much shorter time and of equal value. The indications for their use will be about the same as for suspension, only that they are preferable for corpulent and heavy persons, but on the other hand, they are especially difficult to satisfactorily construct for such patients.

We see, Gentlemen, an almost endless series of means, that indicates usually that they all do little good. That is true, but they all act, as has already been said, more or less excellently in individual cases, and in a disease which is so tedious, often having to be treated for tens of years, it is certainly a good thing to have a large choice of therapeutic aids. You should choose them according to the individuality of the case; do not alter the plan of treatment too hastily,

but proceed patiently with a single method, and try one after the other. As to how this may best be accomplished I will make a few remarks before concluding.

IV.

It now remains for me to refer to the *Indicatio symptomatica*; although so many-sided and important in their nature, though so frequently in tabes, especially in its last stages, will you be compelled, as a matter of fact, to treat symptoms, I can now only briefly touch upon them and refer you mainly to what you already know.

First, with regard to the *lancinating pains*, they require your interference very frequently; sometimes, indeed, they are so slight that they are neglected by the patients, and in these disease often remains for a long time unrecognised, to their detriment.

In all severe forms, however, especially in "tabes dolorosa," with its severe, long-continued and torturing attacks of pain, the patients demand immediate relief. This is often very difficult to obtain; most means do not act with certainty; sometimes this, sometimes that, is required, which means—experiment. Try in the first place the simple external applications: warm or cold fomentations, the application of lint with chloroform or ether upon the hyperæsthetic places, or a chloride of methyl spray, sinapisms, rubbing with chloroform, with veratrine, Spir. formicar., Spir. sinapeos., the application of blistering plasters or opium or belladonna plasters, &c.; further on, electricity: the constant current, the anode or kathode, strong Faradic current with wet electrodes, or Faradic brushing sometimes aid brilliantly; also energetic rubbing or brushing the skin, forcible pressure (bandaging a lead plate upon the skin), massage, suspension, and bloodless nerve-stretching may be tried; lastly, painting with strong iodine or the using of *Pointes de feu* to the spine over the place of exit of the nerve distributed to the specially-affected area.

Usually you will also require to employ internal medication; for instance, the well-tried nerve tonics, quinine,

iodide of potassium, the bromide salts, but more especially the numerous new anodyne drugs. Of them, I place first anti-febrin; but also phenacetin, anti-pyrine, exalgin, salipyrin, salicyliate of soda, lactophenin, &c., may act well. It is sometimes better to give several of these drugs at the same time (for instance, anti-febrin and phenacetin or salipyrin and lactopyrin, or similar combinations) and sometimes they should be combined with small doses of the narcotics (codeia, atropine, morphia). Strong doses of all these drugs rapidly following one another are to be recommended.

Morphia, however, is, and remains, the sovereign remedy, and in all very severe cases you will be hardly able to do without this benefactor to the sufferer, but it is a dangerous matter, for if a patient suffering from tabes has once commenced to take morphia he will almost certainly contract the morphine habit, and with this become doubly unfortunate. Therefore, use the greatest caution with it. The physician alone may give an injection in the severe attacks of pain, for no sooner do you give the patient the syringe in his own hand than there is no more control possible.

Truly there are cases in which the agonies of the patients are so great that their strength is consumed, and it would be unjustifiable to deny them the blessing of morphia. In this the physician's tact, after careful consideration, will guide you to the right course.

Similar and still more difficult is the treatment of other *painful crises* in tabes, especially the *gastric* and *intestinal crises*, which have obviously near relationship to attacks of lancinating pain; in the first place, complete rest is needed, rigid dieting, frequently the entire withholding of food by the mouth (nourishment being maintained by nutritive and salt water enemata); then the anodyne treatment referred to above; warmth, cold, aperients, *Pointes de feu*, are often beneficial, and I have repeatedly found the application of electricity very beneficial (the galvanic current, by means of very large electrodes, applied over the epigastrium and abdomen, over the coeliac, mesenteric, and aortic plexuses, as well as faradisation and faradic brushing over the same regions). Quite recently I have had brilliant success in two cases; usually the hypodermic syringe with morphia is the

ultimate resource. In the intervals between the attacks the debilitated patients must be fed up as much as possible.

In *laryngeal crises*, inhalations of chloroform or ether, the application of cocaine, the galvanisation of the cervical region, the vagi, &c., should be tried; for the ano-vesical and *clitoris crises*, local applications, the bromide salts, antifebrine, codeia, or morphia must be employed.

In the *paræsthesias* and *anæsthesias* you should first try electricity in its various forms. In these cases the faradic, also the labil use of the galvanic kathode, sometimes yield great triumphs. You may also use all kinds of external applications, *e.g.*, rubbing, brushing, massage, &c.

One of the most sad symptoms is the *atrophy of the optic nerves*, and its continuous progress is rarely to be checked. Apart from isolated cases in which I have obtained some success by means of mercury and iodide of potassium, some benefit may be arrived at by long-continued galvanisation, injections of strychnine, application of iodine, and *Pointes de feu* behind the ears and on the neck; success is difficult to judge. The final result was in most—sometimes, however, after years—complete amaurosis. The long-continued subcutaneous injections of cyanide of gold with sodium and cyanide of mercury, recommended by *Galezowski*, I have not tried myself.

The various *paralyses* met with in tabes, especially paralysis of the muscles of the eyes, the atrophic paralysis of the extremities, the tongue, the maxillary muscles, the larynx, &c., are to be treated on well-known general principles—with electricity, strychnine injections, massage, &c. I do not need to enlarge on this.

On the other hand, the treatment of *ataxia* demands a short consideration in respect of recent endeavours to compensate it, and render the patients more comfortable. I will first mention that in all cases where the ataxia has developed rapidly—reached a considerable degree in a few weeks—if it is in any way due to any special exertion, either sexual excess or something of that kind, I am distinctly in favour of insisting upon absolute rest. The patient should, if possible, remain several weeks in bed, or, at any rate, lie down for the greater part of the day, and avoid every exer-

tion as much as possible. I believe that I have benefited many such patients considerably in this way; the ataxia markedly improved. But this must not be carried too far or else greater weakness and laxity of the muscles will ensue, and greater difficulty in meeting the ataxia will follow.

It cannot be doubted that the ataxia can be compensated to a certain extent by the energetic action of the will upon the muscles, concentrating the attention upon the movements, exercising them in definite directions under the control of the eyes, &c. One need only have seen how the patients suffering from ataxia get out of breath and perspire as they strain all their muscles in their attempts to walk, directing their movements with their eyes, in order to realise this.

How much we are capable, through exercise, of strengthening our muscular movements, and of rendering them more fine and exact is known to you all, and in this way an improvement in ataxia is to be gained, taking for granted that the anatomical changes have not too far progressed, and that the motor and co-ordinating nerves are still sufficiently sound. In this case we have obviously to do with a new exercise, perhaps also a re-arrangement of the centrifugal, co-ordinating nerve tracts for the desired movements, as *Frenkel* has already demonstrated. For we can hardly believe that these muscular and movement exercises can have a particular influence merely upon the sensory centripetal nerve tracts.

In such severe cases of acute ataxia as those just referred to, you will do well to take in hand these gymnastic exercises very gradually indeed, to combine them with light massage, and to permit the patients to undertake exercises in walking, &c., only very slowly.

In the common chronic forms of tabes, in which the ataxia has developed to a more or less high degree after the disease has progressed for a long time, you may proceed rather more quickly and more energetically. It is *Frenkel** who has thought out for this purpose very useful methods

* Frenkel, Die Therapie ataktischer Bewegungsstörungen; Münchn. med. Woch., 1890, Nr. 52. Die Behandlung der Ataxie der oberen Extremität; Zeitschr. f. klin. Med., XXVIII., 1895.

and apparatus, which the patients can use in their exercises, in order to gradually reach greater exactitude and certainty in the movements.

For the *legs* we have to employ at first simple movements and forms of movement: bending and stretching, abduction and adduction at the various joints, touching definite points with the toes; to the right, to the left, and slanting movements. Further on, describing circles, following figures drawn upon the floor (circles, squares, hexagons, ellipses, numbers, stars, &c.), or catching balls rolled here and there with the toes, and such like movements. Then follow exercises in sitting down and standing up, bending the knees with and without support, and lastly, standing and walking exercises, standing at first with legs astride, then gradually approximating the feet until they meet; standing upon one foot, on tip-toe, at last even with closed eyes. Walking (led or with a stick, finally alone) in time with exactly measured steps, forwards and backwards, then avoiding obstacles, walking, "toeing the line," round certain figures, &c.

All these exercises, which are at first very fatiguing to the patient, should be done once or twice a day, invariably under the control and psychical encouragement on the part of the physician. At first each single exercise should only be done 5 to 10 times; later on, 20 to 50 times; at the beginning only few, subsequently numerous exercises; this common sense would direct. *Hirschberg* recommends each such gymnastic exercise to be concluded with massage of the legs in order to avoid fatigue.

More delicate and numerous still are the exercises of the *arms* to overcome the ataxia of the arms, which is less seldom met with. For this purpose again *Frenkel* provides a number of apparatus and methods which are very useful. Firstly, single movements of the hands and fingers: bending, straightening, and resistance movements, touching the several finger tips with the thumb, complicated interlacing of the fingers at the same time; tracing figures from copies, guiding a pencil in a more or less deep groove, at length upon a small edge; copying on proper lines, previously drawn, circles or figures; striking objects held before (them), catching swinging balls, touching blocks arranged upon a board

in changing series at the word of command, sticking plugs in holes, sorting wooden disks or coins, finger exercises, as upon the piano and counting out money, and lastly, practising writing and drawing.

It is indeed quite astonishing what progress many patients make in these exercises, how much certainty they regain in walking, how they gradually relinquish their leader and even the stick, and how the symptoms of the ataxia in them become less and less noticeable to the observer; and it is just the same with the hands. In this connection I have just as favourable results to report as *Frenkel*, and have used this method repeatedly during later years with great success. But, again, this method has only a limited sphere of usefulness, and is often tried in vain. In order to gain successful results, great patience is undoubtedly required, also endurance and energy, on both the part of the patient as well as of the physician. It is absolutely requisite that the procedure should be carried out under the continuous supervision of the physician, or of some other intelligent person who possesses a certain amount of authority over the patient.

Disorders of the bladder not infrequently require the interference of the physician. I do not mean catarrh of the bladder, which is to be treated in the usual way, but rather disturbances of innervation, the paresis and paralysis of the bladder; these are primarily to be treated by means of the electric current, according to the well-known methods (but *not* intra-vesical). Further, it may be a question of ergot and strychnine in paresis of the walls of the bladder; strychnine also is useful in weakness of the sphincter, which is usually more troublesome to the patient.

In great weakness of the muscles of the bladder, accompanied by much residual urine, you will be well advised to use the catheter early in the case, but with the greatest precaution, in order to prevent, for as long as possible, the onset of vesical catarrh. If the bladder can be emptied by the pressure of the hand through the abdominal walls, it is preferable. Massage of the bladder may also be tried, and sometimes suspension proves very useful.

Sexual disturbances rarely require special interference. In the initial stages of the disease, heightened sexual desire, or

a tendency to pollution, may sometimes have to be met; this is best done by large doses of bromide, tepid sitz baths, suitable diet, and the avoidance of all sexual excitement. Later on one has rather to meet diminished or abolished power which the patients find very trying. It will be usually best if this power remains in abeyance, as the re-awakening of it might lead the patient to abuse the function; but in some cases it may be advisable to try and cure the impotence. This may be done in the well-known ways—by suitable medical and electrical treatment, by the cautious use of the preparations of strychnine, the "tonic pills," arsenic, &c., and lastly, sometimes with marked results, by suspension.

The *constipation*, which is almost always present, and is usually very obstinate, is to be treated by the usual dietetic and medicinal means, but I advise aperients to be used as sparingly as possible. On the other hand, the physical methods of treatment should be used freely (massage, hydrotherapeutics, and faradisation of the intestines, &c.); *bed-sores* are to be treated on the usual surgical lines, as also the *Mal perforant* (by mercury, iodide of potassium, antiseptic bandages, nitrate of silver, &c.).

Arthropathia tabidorum still requires special mention, although, as a rule, both in the form and use of the joint, the disease progresses deleteriously. Apart from the general treatment of tabes, the methods to be employed in these cases are: placing the joint at rest, moderate pressure by bandages, the application of iodine, and eventually even surgical operation (tapping the joint, resection, &c.). The surgeon's inclination for operative procedures in these cases is not very great, as may be easily understood on account of the difficulty in obtaining healing and the impossibility of removing the root of the disease. Most weight is certainly to be laid upon a suitable orthopædic treatment by means of supporting and protecting apparatus.

I have now finished, gentlemen, with this long, and at the same time not quite complete, enumeration of those therapeutic measures which still play a part in the treatment of tabes. I have intentionally dwelt with some accuracy on these details, because in most text-books you will only find

short references to them, and because I am anxious, in the interests of your future practice, to give you as comprehensive an armamentarium as possible against this wretched disease which will so often require your professional services for many years. At the same time, it is of especial importance to stimulate both the courage and hope of the patient, which is sadly needed in this heavy and wearisome scourge, by decided changes in the treatment through constantly trying new means and methods in order to ensure, at any rate, some measure of success.

And now I wish to say a very few words on the *psychical treatment of tabic patients*, which is of the highest importance, as can be well understood from the very nature of the disease. I strongly counsel you to bear constantly in mind the necessity of as far as possible hiding from the patients the severity and course of their disease, while you rekindle always their confidence and hope and, through your untiring sympathy and care, act favourably upon their spirits. By these means you will render many a patient's burdensome life more bearable, and in this sense will give to suggestive therapeutics, in every allowable way, a particular significance in the treatment of tabes.

It still remains to me, gentlemen, after detailing to you the several curative means and methods which serve us in the treatment of tabes, to shortly give you a *general plan of treatment*, according to which—naturally with many modifications in detail—you may guide your practice amongst tabic patients.

1. *In the early stages* of the disease, if the indications for it are to hand, you will not delay the commencement of an anti-syphilitic course (see page 111), cautiously but still energetically; but do not give too violent a course, rather repeat it several times, utilising a tonic treatment and the application of electricity during the intervals. Then you will have to choose between hydro-therapeutics and spa treatment (either at Nauheim or Rehme, or somewhere else); later—during the winter—use perhaps nitrate of silver and electrical treatment, or possibly try also suspension; side by side of this runs the necessary symptomatic treatment.

2. *In the later stages* you will have to consider well in the

first place whether a mercurial course, alternating with iodide of potassium, is to be instituted; apart from this, to consider the general care and nourishment, and to advise during the summer a stay at a spa or a course of hydrotherapeutics, massage, and electricity; and during the winter gymnastics and massage, suspension, renewed electrical treatment, together with various drugs, should be employed. In connection with all this, the psychical treatment is not to be forgotten.

3. *In the last stages*, finally, it is advisable not to torture the hopeless and helpless patient any more with various cures, spa journeys, electricity, &c., but to limit yourselves to the most necessary treatment of symptoms. At this time the psychical treatment is of the highest value, but at the same time it is also advisable from time to time to institute again some fresh method of treatment. It is now that the human sympathy and tact of the physician has very full opportunity of being utilised.

If I may be allowed in conclusion to give the general impression which the present day treatment of tabes presents, it is this: that we have made, as against former times, very considerable progress in the combat with this wretched disease; we are enabled to meet it with more numerous methods of treatment, and with more certain aim than before; but, notwithstanding this, we have to deplore the still very unfavourable results. Really great successes are sadly rare, and although improved diagnosis teaches us that many a case of tabes remains stationary near its commencement, and that in its rudimentary form the victim of it may live a long life, and not be greatly hindered in his calling or his enjoyment of life, we must still admit that our successes are very slight indeed in the fully-developed and still progressive cases. It is to be hoped that in the future better results lie before us, and that, with an increasing insight into its etiology and character, the hope may arise that our treatment will at length some day conquer the disease.

CONTRIBUTION

TO THE STUDY OF

VISCERAL AFFECTIONS IN THE EARLY STAGES OF SYPHILIS.

I.—ICTERUS SYPHILITICUS PRECOX.

BY

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Late Assistant in the Royal Clinic for Skin Diseases, Breslau.

(*From the Berliner klin. Wochenschr.* 1894. No. 40.)

TRANSLATED

BY

DR. GARROD.

CONTRIBUTION TO THE STUDY OF VISCERAL AFFECTIONS IN THE EARLY STAGES OF SYPHILIS.

I.—ICTERUS SYPHILITICUS PRECOX.

By Dr. O. Lasch.

It has only very gradually come to be recognised that even in its early stages syphilis does not only manifest itself in the form of affections of the skin and visible mucous membranes, but that lesions of other structures, such as the viscera and central nervous system, may also develop comparatively soon after the invasion of the organism by the virus. In this connexion many authors and practitioners have undoubtedly fallen into the error of regarding these visceral forms of syphilis as belonging, as a matter of course, to the tertiary, or gummatous, group, whereas it is beyond question that just as with the cutaneous syphilides, so with the syphilitic changes in all the organs, the papular efflorescences, which are usually early phenomena in point of time, stand in sharp contrast with the gummatous lesions which usually develop years after the infection.

We are far from questioning the occurrence of tertiary gummata, even in the first months and years of syphilis, and merely contend against the assumption, which is so frequently made, as a matter of course, that visceral and gummatous syphilis are synonymous terms. Insistence upon this point seems to me to be important, not from a theoretical standpoint alone, but because it is of very considerable practical importance in connexion with treatment. The tendency to regard all visceral and cerebral syphilitic changes as of a gummatous nature, is very apt to lead to the exclusive employment of the iodine compounds (which have so potent a remedial action in gummatous conditions) in their treatment. If, on the other hand, as may be

assumed from the analogy of the cutaneous efflorescences, we have to deal, in the early visceral lesions of syphilis, with processes, which in their anatomical features and course are comparable with the papular exanthemata, a vigorous mercurial treatment is *à priori* alone indicated. In such cases the administration of iodides appears to us to be, if not superfluous, at any rate only of secondary importance.

Since Ricord wrote—for the scanty scattered records of earlier writers scarcely call for consideration, seeing that they were quickly forgotten—there have appeared, especially in French publications, and with special frequency of recent years, accounts of visceral affections in the early stage of syphilis. It is true that these deal, for by far the most part, with cerebral affections, and only to a small extent with those of the kidneys, liver and other organs. In Germany also cerebral syphilis has attracted most interest during the last twenty years, whereas reports on affections of the kidneys, and still more of the liver, occupy an altogether minor place.

In all the German literature I have failed entirely to find any reference to the occurrence of benign jaundice in the early stage of syphilis, with the exception of two cases reported by Engel-Reimers*†, and the debate at the last Congress für Innere Medicin, whereas I have been able to collect more than forty cases from French sources, which are embodied in a small table at the end of my paper.

It is the same with the text-books—whereas Fournier‡ and especially Mauriac§, each devote a chapter to this condition, it is only very briefly referred to by Lang‖, Kaposi¶, Finger** and Baümler††, and is passed over in complete silence by Zeissl.

Although cases of syphilitic jaundice are apparently some-

* Engel-Reimers: Ueber acute gelbe Leberatrophie. Jahrb. d. Hamb. Staatskranken. Anstallen, 1889.

† Engel-Reimers: Ueber die visceralen Erkrankungen in der Frühperiode der Syphilis. Monatsh. f. prakt. Dermat., 1892.

‡ Fournier: Leçons cliniques sur la syphilis. Paris, 1884—86.

§ Mauriac: Syphilis tertiaire et héréditaire. Paris, 1890.

‖ Lang: Vorlesunger über Pathol. u. Therapie der Syphilis. 1884—86.

¶ Kaposi: Pathol. u. Therapie der Syphilis. 1891.

** Finger: Die Syphilis u. d. vener. Krankh. 1892.

†† Baümler: Syphilis. 1886.

what rare (and from my study of the material afforded by the Breslau clinic, I cannot confirm Engel-Reimers' statement that benign jaundice occurs in two per cent. of all cases of syphilis), this cannot be the sole reason for the scantiness of the records of such cases in Germany. The explanation is rather to be sought in the fact that the patient, as a rule, consults his usual medical attendant to whom he says nothing of his syphilitic affection, and seeing that (as we often find stated in the literature) the jaundice may completely mask the accompanying rash, the cases of (probable) syphilitic jaundice naturally pose as examples of the catarrhal variety, and so do not get referred to the special group to which they belong.

Moreover, doubt has been expressed even, for example, by Lang and Kaposi, whether, in such cases, we have to deal with a specific affection, and not rather with catarrhal jaundice in syphilitic subjects.

In opposition to such doubt, however, I believe that one may draw a special clinical picture of syphilitic jaundice, seeing that it presents several distinctive features, which I have been able to confirm with a certain degree of constancy and regularity in nearly fifty cases.

The more familiar one becomes with such cases the more will the diagnosis of syphilitic jaundice appear justified, and to illustrate this, I purpose giving here accounts of three cases occurring in the early stages of the disease, two of which are derived from the Royal Dermatological Clinic in Breslau, the third from the private practice of Prof. Neisser, to whom I tender my heartiest thanks for his kind permission to make use of it.

In addition to these three cases recently observed, I have found, on going through earlier notes of the Breslau clinic, ten other cases in which it is stated that jaundice developed in patients suffering from the early stages of syphilis in association with rashes, mucous tubercles, etc. Since, however, the notes alluded to are not sufficiently complete for my purpose I will content myself with merely mentioning this fact.

I look upon the following features as differentiating ordinary catarrhal jaundice from the syphilitic variety:— Syphilitic jaundice is usually of quite sudden onset, and

is not preceded, as the catarrhal is, by symptoms of digestive disturbance, such symptoms being often entirely absent throughout its course. Food is taken with a hearty appetite, and the nourishment taken is well assimilated, but as is readily explicable, the distaste for all fat is shared by the two classes of patients. That in some cases of syphilitic jaundice the patients suffer from loss of appetite and nausea, is easily understood, for we know that such disturbances are among the commoner symptoms of the eruptive period of syphilis. It is also a matter of frequent observation that, after the sudden onset of the jaundice, digestive disorders eventually develop, in association with such other disturbances of the general health as often accompany the first appearance of the rash.

A further diagnostic feature is the absence of any other cause, a point which we find specially noted in all these cases. If it be objected that we have frequently to deal with alcoholic subjects, or persons of irregular life, in whom digestive disorders may often be observed after slight provocation, or with no ascertainable cause apart from syphilis, it may be replied that cases have also occurred in which jaundice has developed in hospital on a well regulated diet.

As to course and duration there is nothing characteristic, seeing that the duration of an attack of syphilitic jaundice varies from three weeks to three months, which is about the same as that of the catarrhal form, in which also as long a course as this is known to occur. On the other hand, it seems to me that we are justified in taking into consideration the effects of treatment in support of the diagnosis, since almost all reports agree in stating that the non-specific treatments (Rhubarb, Carlsbad Salts, etc.), which are usually at first employed, have had no effect, until anti-syphilitic treatment, either by mercury alone or combined with iodide was substituted and quickly brought about an improvement. It is of special interest to point out that in some cases, after a too early stoppage of mercury, jaundice which had already disappeared has returned, and a definite cure has only been obtained by a renewal of the mercurial treatment.

The objection which has been raised, by English authors chiefly, that the jaundice is not due to the syphilis but to

the mercury, may be regarded as completely disposed of by such observations, and by the fact among the fifty cases there were only three or four in which mercury had been administered before the onset of the jaundice.

What is, however, of the greatest importance from the point of view of diagnosis is the regularity with which the jaundice appears at the same period of syphilis simultaneously with the first development of the rash. Indeed, the coincidence of the jaundice with other syphilitic manifestations appears to me to be so important that without it one is not justified in speaking of a syphilitic jaundice.

It will be seen that among thirty cases in which I was able to find the time stated, jaundice developed in the second, third or fourth month after the appearance of the primary affection in twenty-five, and that in the other cases there was always simultaneously present a belated or relapsing exanthem (in one case the third crop of roseola). This constant association certainly lends little countenance to the view that we are here dealing with a catarrhal and not with a specific jaundice.

In attempting to answer the question: "How is the development of jaundice on the basis of the syphilitic disease to be explained?" one is met by a twofold difficulty. The first obstacle in our path is our defective knowledge of the virus of syphilis, and the impossibility of communicating it to animals, which stands in our way here as in every attempt to explain the manifestations of syphilis, their distribution in the organism, and the whole nature of the disease.

In the second place *post mortem* observations, which in cases of tertiary syphilis often contribute to the elucidation of the pathological processes, are here wanting. With the exception of cases of *icterus gravis* in the early stages of syphilis, of the occurrence of which a few observations (by Engel-Reimers and others) with *post mortem* reports are available*, I have only been able to find two accounts of

* I am indebted to Professor Neisser for a verbal account of the following case of which I have not been able to obtain the *post mortem* notes. A female patient was admitted to hospital with obvious early symptoms of syphilis. She had at the same time jaundice of moderate degree. She was placed on a course of mercurial treatment, during which acute yellow atrophy of the liver developed and proved fatal.

autopsies upon individuals who have died of other diseases whilst suffering from early syphilis, and in whom changes in the liver were found *post mortem*.

1. Key* reports that in the case of a woman, aged 26, who died of miliary tubereulosis (and who had been treated six months before her death for a primary sore on the right *labium majus*), he found in the right lobe of the liver, just at the surface, a gumma as large as a walnut. The microscopic structure, even to the unusually scanty connective tissue growth in the neighbourhood, was exactly that of an ordinary hepatic gumma.
2. Fleischhauer† related at the last Congress für innere Medicin a case in which, after infection in August, 1872, severe jaundice developed in October, 1872, which yielded to mercury and iodide. In February, 1873, death occurred from erysipelas, and *post mortem* a gumma was found in the liver.

In the first case (of which I have only been able to consult an abstract), all data are wanting as to the previous symptoms and course of the syphilis, and also information as to whether during life any symptoms of hepatic disease were observed. The presence of jaundice may, at any rate, be excluded on account of the situation of the tumours. Neither case is of much use from our point of view, the "gummata" are very remarkable, and in other respects too they depart widely from the category of other observed cases of benign jaundice. I have, however, alluded to them for completeness' sake.

The attempts at an explanation which have been published by various authors, rest upon purely theoretical bases.

Lancereaux‡, and with him Quinke§, Keyes‖, and Engel-Reimers believe that the jaundice is due to compression of the bile ducts by the portal glands, which, like the palpable peripheral lymphatic glands, are conspicuously swollen owing to the general infection of the organism.

* Ref. Schmidt's Jahrbücher, 1874, B. 161.
† XII. Congress f. innere Medicin. Wiesbaden, 1893.
‡ Lancereaux: Traité historique et practique de la Syphilis, ii. 1873.
§ XII. Congress f. innere Medicin. Wiesbaden, 1893.
‖ Keyes: Genito-urinary diseases with Syphilis. 1888.

This hypothesis apparently receives support from the *post mortem* appearances in a syphilitic patient who died of *icterus gravis*, in whom Engel-Reimers found quite unusually enlarged groups of glands in the hilum of the liver; and also by the clinical observation that jaundice is specially apt to occur in patients who exhibit the multiple chain-like glandular swellings, which are described by French authors under the name of "Chapelets de la vérole." The fact that the glands are only very slowly influenced by anti-syphilitic treatment is also perhaps in favour of this view, for to this cause may be ascribed the slowness of the recession of the jaundice and hepatic enlargement which is frequently observed.

On the other hand it must be pointed out that the swelling of the glands in the hilum of the liver occurs at about the same period as that of other glands not primarily involved, and consequently it is hard to say why in some cases the compression of the bile ducts has only occurred in the tenth month.

Gubler* (with whom Baumler, Senator† and Chapolet‡ agree), seeks to explain the jaundice by supposing that in the deeper-seated mucous membranes the same changes occur as in the skin and visible mucous membranes, and that (leaving aside differences due to the different anatomical conditions) eruptions or roseola and of papules occur on the mucous membrane of the biliary passages, which lead to swelling of the mucous membrane, and so to blockage, or at least partial obstruction, of the bile ducts.

The chief point in favour of this view is the coincidence of the jaundice with the appearance of the rash, and the fact, specially brought out in almost all the published cases, that unusually abundant eruptions were present, in association with which the jaundice made its appearance.

On the other hand Mauriac§, and with him a number of

* Gubler: Mémoire sur l'ictère qui accompagne quelquefois les éruptions syphilitiques précoces. Mém. de la Société de Biologie, 1853. Tome I.

† XII. Congress f. innere Medicin. Wiesbaden, 1893.

‡ Chapolet: Trois cas d'ictère survenue pendant la période secondaire de la syphilis. Lyon Méd., 1891.

§ Mauriac: Syphilis tertiaire et héréditaire. Paris, 1890.—Syphilis secondaire du foie. Gaz. Hebdom. de Méd. et Chir. 1888.

French writers, hold that an affection of the liver is the primary event, and that the biliary passages are only secondarily involved. He, therefore, sets up, as a postulate for the diagnoses of syphilitic jaundice, the presence of hepatic enlargement, with or without pain. According to him we have to do with a true inflammatory process in the liver. Here, as in gummatous syphilis of the liver, there is present hypertrophy of the organ due to diapedesis of white corpuscles and proliferation of fibrous tissue corpuscles; in contrast, however, to gummatous disease there is here no tendency to organisation and gumma formation, but resoeption eventually takes place and no permanent damage results. "The hyperæmic process spreads to the biliary passages and gives rise to proliferation of newly-formed epithelial cells and to desquamation of the old ones, which latter act as a plug causing obstruction of the bile ducts, and so producing jaundice."

In proof of the correctness of this view he brings forward cases in which hepatic enlargement was present, which receded without the development of jaundice, such as that recorded by Lacombe*, and also those cases in which enlargement of the liver precedes the jaundice.

Finger regards the jaundice as a toxic phenomenon due to the syphilis toxin, but the criterion which he sets up, that the toxic phenomena yield promptly to iodide, whereas they prove more refractory to mercury, here fails; for the jaundice, according to all reports, resembles other infection-symptoms in being markedly ameliorated by mercury, whereas iodide alone remains without effect, as with the manifestations of secondary syphilis which are due not to poisoning, but to direct bacterial action.

Quedillac†, to whose hypothesis I will refer for the sake of completeness, holds (like Ricord, who refers the jaundice to an alteration in the organism caused by the entrance of the syphilitic virus into the blood) that the blood being altered by the presence of the virus causes an irritation of the epithelium of the biliary passages, a catarrh, which results in desquamation of the cells, and so to obstruction of the bile-streams.

* Thèse de Paris. 1874.

† Quédillac: Thèse de Paris. 1885.

It is clear, without further argument, from the above exposition, that all the attempts at explanation referred to, rest upon very insecure bases. An explanation of the pathogenesis of syphilitic jaundice grounded upon positive facts is still wanting, and consequently it is not definitely proved that jaundice in syphilis is a specific jaundice due to the syphilis.

Before proceeding to give a brief tabular summary of the forty-nine cases at my disposal, I propose to describe shortly the course of the cases which I have myself observed.

Case. I.—A. F., a female patient, aged 19, attended at the Medical Polyclinic at this place on September 5th, 1892, on account of jaundice. Thence she was referred to the Dermatological Polyclinic on account of an ulcer on the posterior commisure of the labia majora. This ulcer, which was as large as a pea, secreted very little, was situated upon a parchment-like infiltrated base, and gave the impression of being a primary sore on the way to healing. The inguinal glands were greatly swollen, but painless, and there was also obvious swelling of the glands of the forearms and neck. Since June 25th, 1892, the patient had had sexual intercourse with her bridegroom, who had been infected with syphilis a year previously. The patient had noticed the ulcer at the end of July. At first only local treatment of the ulcer was carried out, and Carlsbad salts and a restricted diet were prescribed on account of the jaundice, which had only been present for one day. During the following days the jaundice increased, pains in the limbs, "malaise" and a slight rise of temperature developed, but the appetite remained good. The liver was somewhat enlarged.

September 10*th*.—Jaundice very intense. General condition worse. Eruption of a very abundant maculo-papular rash on the trunk, head, and limbs. The ulcer is almost completely healed. Patient was to have been admitted, but stayed away in spite of her promise, and only presented herself for admission on the 28th. The ulcer was then healed, there was much general glandular enlargement, and a very pronounced maculo-papular rash. The jaundice had increased, the urine contained bile-pigment, and the fæces were colourless. The liver was somewhat tender on pressure and enlarged; there was slight enlargement of the spleen. General condition fairly good; appetite good, and merely a distaste for fatty foods. The patient received daily injections of 0·01 grm. perchloride of mercury.

October 9*th*.—The jaundice has almost disappeared, but there is still a slight bile-pigment reaction in the urine. Fæces darker. General state good. Liver of the same size but no longer tender. Rash entirely disappeared.

October 18*th*.—In the sclerotics alone there is still a distinct icteric

tint. Urine free from bile pigment. Liver smaller. Severe nocturnal headache—3 grm. iodide of potassium and 2 grm. bromide of potassium, with equal quantity of antipyrin.

October 29th.—Feels very well: has gained eight pounds in weight. Jaundice completely disappeared. Liver within its natural limits. Headache better. Patient discharged, having had in all 30 injections (each of 0·01 grm.) of perchloride and 15 grm. of iodide of potassium.

I have seen the patient on several occasions since, and she has never shown any obvious syphilitic symptoms, nor has she had any return of jaundice. She says that she has been free from illness in the intervals.

In my opinion the following features render diagnosis of syphilitic jaundice a very probable one in this case, viz.:—the absence of any other cause for the development of the jaundice and its long duration; the hepatic enlargement; the simultaneous outbreak of an abundant maculo-papular rash, and the improvement after the adoption of anti-syphilitic treatment, accompanied by the disappearance of the other symptoms.

Case II.—Hugo G. Moulder, aged 26. In the middle of July the patient had a primary sore for which only local treatment was applied. At the end of October a rash developed, and, in the beginning of November, jaundice.

On November 14th he was admitted to the clinic. Present condition—Remains of the primary lesion on the *dorsum preputii*; general glandular enlargement; a severe maculo-papular rash; intense jaundice, and well-marked enlargement of the liver. The boundaries of the liver were as follows: above, the sixth intercostal space, below, as was clearly shown by percussion, from three fingers' breadth below the costal arch in the anterior axillary line, and four fingers' breadths from the parasternal to the left nipple line. By palpation the lower border of the liver can be felt a hand's breadth below the ribs. Spleen somewhat enlarged and palpable. The diameter, as made out by percussion, was 7·9 cm. Urine free from albumen, but yielding a very pronounced bile-pigment reaction.

Motions clay coloured.

Slight sensation of weight and pain in the right epigastrium. No nausea. Appetite good.

Treatment: Sweating, Carlsbad salts and rhubarb.

November 16th.—From this day onward daily injections of 0·01 grm. perchloride of mercury.

November 21st.—Jaundice rather less marked, liver smaller, from this date 0·02 grm. of perchloride daily.

November 23rd.—Stomatitis. Mercury stopped.

November 30th.—Stomatitis cured. An injection of 0·02 grm. perchloride.

December 3rd. — Jaundice much better. Motions coloured, liver smaller, splenic enlargement disappeared.

December 7th.—Severe stomatitis; since yesterday salivation; mercury stopped.

December 13th.—Mercury resumed to-day. Jaundice more marked.

December 17th.—Patient was discharged at his own request before the completion of the cure. The rash is completely gone; the jaundice is much diminished; the fæces deeply coloured and the liver smaller but still somewhat enlarged.

Although instructed to come as an out-patient for further injections the patient did not put in his appearance again.

Here again we have jaundice appearing after the eruption of an abundant maculo-papular rash, and not preceded by any digestive disturbance, which was caused to disappear as the result of a repeatedly interrupted mercurial course. I think that the incompleteness of the cure must be ascribed to the impatience of the patient who would not stay for the completion of the anti-syphilitic course.

Case III.—Wilhelm B., tradesman, aged 26. The patient suffers from very frequently recurring herpes of the genitalia, which he has been accustomed to treat for himself, and we may readily assume that in consequence of this a primary syphilitic lesion was overlooked.

At the end of April the patient was attacked with severe headaches, with marked nocturnal exacerbations, and the eruption of a papular syphilide very soon followed.

At the end of May moderately intense jaundice developed, accompanied by somewhat acute pain in the right epigastrium, but without any antecedent digestive disturbance. The liver was enlarged.

In the beginning of June the jaundice persisted with undiminished intensity, there was a very abundant papular syphilide on the body and an impetiginous syphilide on the head, together with mucous tubercles on the tongue.

In the middle of June the patient was sent by Professor Neisser to Wiesbaden to undergo a thorough anti-syphilitic treatment under the care of Dr. Tonton. The latter was kind enough to inform me that the patient underwent a course of 30 inunctions (10 of 3 grm. and 20 of 4 grm.), and that during this course all the symptoms, rash, jaundice, hepatic enlargement and plaques disappeared.

In the middle of July the patient returned to Breslau. I have myself repeatedly seen him since, and know that, with the exception of mucous tubercles which appeared in September, he has had no obvious manifestations, and has continued in good health.

Summing up this morbid history we see that in a case in which the date of infection was unknown, jaundice with hepatic enlargement developed shortly after the eruption of an abundant papular exantheno, and yielded completely to anti-syphilitic treatment.

I now present the tables of forty-six cases collected from published sources, and my own three cases.

From this tabular epitome (from which, however, Chapolet and Salmone's* cases are missing which were not accessible to me in the original, and which are too briefly summarised in the abstracts), we see that syphilitic jaundice occurs with nearly equal frequency in women and in men. Since, however, we know that the number of syphilitic men, who come under observation, is greater than that of the syphilitic women, we must conclude that jaundice is a more frequent symptom of the eruption-period in women than in men. This observation is in complete accord with the teaching of experience that women are liable to specially severe eruptive symptoms.

The points of view presented above are almost everywhere borne out by the tables, viz.:—The regularity of the onset of the jaundice in the early period of syphilis, simultaneously with the development of rashes, and usually of exceptionally profuse rashes; the rapid improvement under mercurial treatment, and the absence of digestive disturbances.

It seems to me that the chief importance of this jaundice in the early stages of syphilis lies in the domain of treatment, seeing that it is by a well-timed resort to anti-syphilitic treatment that we can render the most rapid and certain aid to the patient. It is also, perhaps, a point to be considered whether (as some authors have held with regard to other syphilitic processes), when the cases are inadequately treated, a focus may not persist which may, at some later period, form the starting point of a gummatous growth.

Again we must take into consideration the possibility that cirrhotic processes may have their starting point in the hyperæmic and inflammatory processes which are held

*Giorn. med. dell' exercita et della mar. Feb., 1892. Abstract: Journ. des maladies cutan. et syphil. 1893.

responsible for the development of the jaundice. In conclusion I will consider briefly the question whether mercurial treatment may not exercise an injurious influence upon the hyperæmia and inflammatory processes in the liver which accompany the jaundice. That case in particular, mentioned above in a foot-note, which Professor Neisser had the opportunity of seeing, may well raise the question whether in that particular instance the energetic mercurial treatment employed may not have produced the acute yellow atrophy.

However, such a notion has neither a clinical nor a sound experimental basis. I do not propose to enter into the whole literature of the effects of the long administration of small doses of mercury, and will only mention the most recent investigations, published by Ullmann*, which show that in one case after the assimilation of mercury (in quantities such as are employed in an ordinary anti-syphilitic course) a fresh callus, or chronically inflamed hyperplastic bone, yielded a much more distinct mercury reaction than did healthy bones.

Yet, as Ullmann himself admits, one is hardly justified from this single experiment in regarding it as certain that inflamed structures exercise a greater power of attracting the drug than those which are in a normal condition.

Ullman's experiments have, undoubtedly, shown that, next to the kidneys, the liver was, of all the remaining organs, that in which most mercury could be detected, and that this organ appears to take the metal to itself from the circulating blood very rapidly, and only to excrete it again very slowly. Nevertheless in chronic mercurial poisoning, as it is especially seen in people who, in the course of their occupation, have continually to do with mercury, or are compelled to inhale its vapour, affections of the liver are much more rarely met with than those of other organs (kidney, intestine, heart, &c.). Accordingly we may rightly conclude that injury to the liver, even when it is in a pathological condition, need not be expected to result from a judiciously conducted mercurial treatment. Otherwise we should

* Ullmann: Ueber die localisation des Hg. im thierischen Organismus, &c., Archiv f. Dermatol. u. Syph. 1893. Ergänz, Heft II.

certainly very frequently be confronted with malignant degeneration of the liver, instead of seeing in so large a number of cases cure and improvement of the jaundice under treatment by mercury.

LASCH'S TABLE OF FORTY-FIVE CASES OF SYPHILITIC JAUNDICE.

No.	Author's Name.	Primary Affection.	Jaundice.	Concomitant Syphilitic Symptoms.	Course.
1	Percy (quoted from Gubler) (man).	(?)	(?)	Still the primary affection and exanthem.	Jaundice not influenced by mercurial pills, but jaundice and rash cured by 20 mercurial inunctions.
2	Ricord* (man)	---	Sudden onset 2 months after primary affection.	Very abundant maculo-papular rash, with squamous and pustular efflorescences.	Jaundice disappeared before the rash after pills of protiodide of mercury.
3	,, ,, ...	——	4 or 5 weeks after the primary affection.	Papulo-squamo-pustular syphilide with impetiginous areas.	Jaundice of almost maximum intensity, which did not disappear for 4 months.
4	Gubler (man).....	——	10—12 weeks after the primary affection, preceded by digestive disturbance.	A papular syphilide developed a few days after the jaundice.	Jaundice cured before the papular syphilide.
5	,, ,, ...	(?)	Mid-September	Roseola and papular syphilide	Jaundice disappeared before the syphilide.
6	,, ,, ...	(?)	(?)	Simultaneous rash and jaundice	Both symptoms yielded quickly to mercury.
7	,, ,, ...	——	2 months after the primary affection.	Rash, alopecia	Not stated.
8	Gubler (woman—gravid).	(?)	(?)	Papular-pustular-crusted syphilide.	——
9	Foville† (woman)	Sept 16, 1856	Oct., 1857	Dec. 16, 1856, macular rash. Mar. 31, 1857, second macular rash. Oct., 1857, third outbreak of roseola, soon after the jaundice.	Jaundice disappeared in 10—12 days on mercury, and the roseola as quickly.
10	Mauriac (man)	Jan., 1876	Beginning of April	In the middle of March violent prodromal symptoms, roseola, jaundice 10 days later.	On 8th day jaundice very intense, liver enlarged, rash in spots larger than franc pieces, impetiginous pustules on head. On 24th day commencing improvement. On 30th day rash and jaundice cured.

*Ricord: Clinique iconographique de l'Hôpital des Vénériens. Paris, 1851.

†Foville: Observation de syphilis constitutionnelle avec zona et ictère.

LASCH'S TABLE—*continued.*

No.	Author's Name.	Primary Affection.	Jaundice.	Concomitant Syphilitic Symptoms.	Course.
11	Luton (quoted from Mauriac) (man).	(?)	70 days after primary affection pains in hepatic region; 4 days later jaundice.	Widespread roseola, plaques on the tonsils.	——
12	Luton (quoted from Mauriac) (man).	——	9 months after the primary affection very intense jaundice with enlargement of the liver.	Macular syphilide, mucous tubercles.	Discharged cured after 4 weeks.
13	Lacombe (quoted from Mauriac) (woman).	——	7 months after the primary affection enlarged liver and jaundice.	Roseola, plaques, alopecia; exostoses on forehead, tibia, and clavicle.	Jaundice lasted 17 days, the hepatic enlargement 2 months.
14	Quinquand*	——	Jaundice, enlarged liver...	Rash, nocturnal headaches ...	Almost 4 months elapsed before complete recovery.
15	,, (man).....	——	Slight enlargement of liver, slight jaundice.	Malignant syphilis, ulcerative skin affection.	Recovery in 18 days.
16	,, ,, ...	——	2 months after the primary affection.	Severe prodromal symptoms, pustular syphilide developing on the roseola.	With increase of the jaundice change in the roseola. On the 16th day improvement in all symptoms.
17	Lancéraux (man)	——	7 weeks after the primary affection.	Roseola 6 weeks after the primary affection.	Jaundice better after 3 weeks; roseola disappeared; jaundice cured after 6 weeks.
18	,, (woman) ..	End of Feb.	Apr. 12..... ...	Apr. 11. papulo-lentienlar syphilide, alopecia, mucous tubercles, ulceration left labium major.	Apr. 14, jaundice more marked. Apr. 17, jaundice still more intense. Apr. 28, jaundice better. May 1, jaundice disappeared.
19	,, (man)	(?)	(?)	Mucous tubercles, syphilitic angina, jaundice.	Nothing known as to the course of the jaundice.
20	,, ,, ...	?)	(?)	Roseola, plaques, headache, jaundice.	Do.
21	,, ,, ...	(?)	(?)	Roseola, plaques, papules, jaundice.	Do.
22	Biermer (quoted from Lanecéraux) (woman).	(?)	(?)	Roseola, jaundice	Liver enlarged. Cure by mercury.

* Quinquand: Les affections du foie. Paris, 1879. Vol. 1.

No.	Author's Name.	Primary Affection.	Jaundice.	Concomitant Syphilitic Symptoms.	Course.
23	Quinquand (woman)..	(?)	Developed after 6 days' stay in hospital.	Rupia, ecthyma, jaundice, hepatic enlargement.	In 3 weeks rupia and jaundice cured. Rapid relapse, and later a second relapse. Definite recovery in 4 months.
24	,, ,, ...	——	4 months after primary affection.	Very severe roseola and papular rash, pap. ad genit., liver enlarged.	On 12th day rash fading, liver smaller. Jaundice disappeared only after 3 months. Liver again normal.
25	Schröder* (man)	Mar., 1886	Oct. 1	In July, 1886, papular syphilide. In Aug., 1886, syphilitic ulceration. Oct., 1886, ulcer covered with a crust on the face; rash, papules on head, alopecia, condylomata at anus. Primary sore (?) not yet healed.	Oct. 24, jaundice still much the same. Nov. 1, rash disappeared, jaundice better. Nov. 4, jaundice slight. Nov. 7, jaundice gone.
26	,, ,, ...	Oct. 25, 1886	Feb. 1, 1887	Macular rash in Oct., 1886. No other symptoms.	Perchloride injections at first. After 3 days jaundice less, after 7 days jaundice gone. Injections stopped, liq. van Swiet: substituted. Mar. 2, jaundice relapse; 5 teaspoonfuls of liq. van Swiet: Mar. 4, jaundice gone.
27	,, (woman) ...	End of Nov., 1886	Middle of Jan., 1887. Moderately intense.	Mucous tubercles of mouth and vulva, palmar and plantar syphilides.	Injections of hg. peptone. Jan. 20, jaundice increased. Feb. 1, jaundice better. Feb. 10, cured.
28	,, (man)	End of Jan., 1887	Mar. 18, 1887	At the end of Feb., 1887, roseola and very abundant papules.	Injections of hg. peptone. Mar. 5, jaundice less. Mar. 21, jaundice gone, roseola slowly fading. Apr. 4, maculer eruption all over body. Apr. 18, exanthem cured.
29	,, (woman) ...	Sept., 1886	Feb., 1887	Mucous tubercles on throat, palmar and plantar psoriasis, macular rash.	Mar. 24, jaundice less. At the beginning of May jaundice and papules gone.

* Schröder: De l'ictère syph. second. Thèse, 1887.

LASCH'S TABLE—*continued.*

No.	Author's Name.	Primary Affection.	Jaundice.	Concomitant Syphilitic Symptoms.	Course.
30	Schröder (woman) ...	(?)	(?)	Condylomata on genitalia and about anus, mucous tubercles, jaundice.	Recovery after 15 days.
31	,, (man)	Nov., 1882	Jan., 1883	Splendid roseolous rash	Feb. 24, jaundice gone, still traces of roscola.
32	Lacomble (quoted from Moulard) (woman).	On the lip, Dec. 8, 1872.	Feb. 27, 1873	Feb. 25, fever, mucous tubercles. Feb. 27, isolated papules. Mar. 5, papular rash over whole body.	Mar. 6, jaundice better. Mar. 13, patient well.
33	Monlard* (woman) ...	——	June 16	June 15, rash. June 27, intense jaundice, very abundant papular corymbose rash, coryza, plaques.	Intercurrent erysipelas. July 17, jaundice disappeared. July 22, patient well.
34	,, (man).....	——	June 6, 1879	——	June 12, jaundice more intense. June 21, jaundice less, lenticular roscola. Cure by mercury.
35	,, (woman).....	Aug. 13	Oct. 7	Sept. 27, condylomata on anus and genitalia.	Oct. 1, vomiting. Oct. 5, gastric disturbance gone. Oct. 6, renewed vomiting. Oct. 7, jaundice. Oct. 22, jaundice and condylomata cured.
36	,, ,, ...	Sept., 1878	Feb. 12, 1879, without any cause.	Feb. 2, abundant papular rash	Feb. 28, jaundice better. Mar. 7, jaundice and rash cured.
37	Quedillac (man)	Oct., 1881	Jan. 15, 1881	No antisyphilitic treatment. Jaundice worse. Feb. 8, condylomata, papules.	Feb. 8, mercurial treatment. Feb. 17, cutaneous symptoms and jaundice gone; mercury stopped. Aug. 7, fresh jaundice; mercury given. Aug. 27, jaundice cured. In 1883 three attacks of jaundice simultaneously with rash and mucous tubercles.

* Moulard: Thèse de Paris, 1879.

No.	Author's Name.	Primary Affection.	Jaundice.	Concomitant Syphilitic Symptoms.	Course.
38	Quedillac (man)	Feb. 1	June 1	June 1, eroded papules on the toes, condylomata at anus, palmar psoriasis.	July 5, jaundice more intense. June 10, jaundice better. June 12, cured; mercury stopped. June 22, relapse of jaundice. June 23, jaundice disappeared.
39	,, (woman) ...	Apr., 1882	Aug. 14, 1882	June, maculo papular and pustular rash. July 31, specific sore throat. Aug. 4, still scattered papules.	Aug. 25, jaundice less, syphilide cured. Sept. 4, jaundice still present, return of syphilide. Oct. 30, patient cured.
40	,, ,, ...	June, 1882	Aug. 3, 1882	July 22, genital papules, maculo-papulo-pustular rash. Aug. 31, rash better.	Aug. 7, jaundice still present. Aug. 14, jaundice and syphilide almost cured.
41	,, ,, ...	Oct., 1883	Sept., 1884	Syphilitic rash; ulceration, which had destroyed the posterior wall of pharynx and the uvula.	Oct. 15, jaundice almost gone.
42	,, ,, ...	——	——	Condylomata on genitalia and at anus, jaundice.	Recovery under mercurial treatment.
43	Chabannes* (woman).	——	——	Papular rash, jaundice	A fortnight later papules had ceased to form; 12 days later jaundice and skin symptoms cured.
44	Engel-Reimers (woman)	——	May 29, jaundice	May 12, anal condylomata. May 22, cured. June 1, very distinct jaundice, copious small roseolar rash.	June 4, jaundice increasing. June 11, jaundice better, roseola gone. June 21, jaundice gone.
45	,, ,,	——	Nov. 7, 1885	Nov. 7, condylomata on genitals, mucous tubercles on tousil.	Nov. 13, jaundice more intense. Dec. 6, jaundice gone.

* Chabannes: Observation d'un ictère ayant accompagné une éruption syphilitique précoce. La Province Méd., 1887.

LASCH'S TABLE—*continued.*

No.	Author's Name.	Primary Affection.	Jaundice.	Concomitant Syphilitic Symptoms.	Course.
46	Lacombe (quoted from Mauriac on Tertiary Syphilis) (woman).	——	7 months after primary affection.	Roseola. plaques. shortly after exostoses on forehead and clavicles.	Mercurial treatment; jaundice disappeared in 15 days.
47	Own case. F (woman)	July, 1892	Sept., 1892	Very abundant papular rash...	Jaundice cured in 8 weeks. (*Vide supra*, Case 1.)
48	„ F (man) ...	„ „	Nov., 1892	Abundant macular rash	Jaundice almost gone after 4 weeks. (*Vide supra*, Case 2.)
49	„ B „ ...	(?)	May, 1893	Abundant papular rash; mucous tubercles.	Jaundice disappeared after 6—8 weeks, after thorough mercurial course. (*Vide supra*, Case 3.)

SYPHILIS AND GENERAL PARALYSIS IN ICELAND.

BY

DR. EDWARD EHLERS,

Of Copenhagen.

Extract from "Chronicles of Dermatology and Syphilography."

TRANSLATED

BY

DR. GUTHRIE RANKIN.

SYPHILIS AND GENERAL PARALYSIS IN ICELAND.

By Dr. Edward Ehlers.

It was at one time believed that some nations were secure against syphilis, and until lately this belief was widely maintained as still true in regard to the inhabitants of Iceland. Mackenzie has called attention to it, and his observations have been confirmed by Thorsteinssen and Jacotot, and recapitulated in the works of Hirsch and others. An absolute immunity has not been claimed by these writers, but they have contended that the disease is incapable of becoming established in the island on account of the simple and pure habits of the population. This opinion has also been held by Jullien and Lesser.

In 1891 Lesser endeavoured to throw light upon this contention in a letter addressed to Dr. Schierbeck, Principal Medical Officer of Iceland, whose reply was published in the "Archiv für Dermatologie und Syphilis," 1891, p. 37.

The questions to which Lesser requested an answer were :—

1. Is it true that syphilis does not exist among the Icelandic population of the present day ?

2. Are records not found of the appearance of *morbus gallicus* in Iceland in the literature of the island belonging to the end of the fifteenth and beginning of the sixteenth centuries, that is to say of the period during which the first epidemic of syphilis spread throughout Europe ?

In his answer, Dr. Schierbeck has related his experience during eight years, in the course of which there were brought under his observation four undoubted cases of syphilis, one patient whom he suspected of having contracted the disease, and one characteristic case of general paralysis.

Case No. 6.—*A married man. No children. Six years' residence abroad. It is uncertain whether the patient has had syphilis, but, in his youth, he is admitted to have led a fast life.*

A typical case of general paralysis. Death two years after the appearance of the first symptoms.

All Dr. Schierbeck's patients had contracted their syphilis abroad.

Schierbeck very properly remarks that the local conditions, the thinness of the population, and the familiar mutual intercourse between the inhabitants of any one place and their immediate neighbours make it highly probable that an importation of syphilitic virus would be immediately discovered.

Syphilis is imported into Iceland both by the natives and by strangers.

The native importers of syphilis belong to the well-to-do classes; the poor are not possessed of the means which would enable them to travel.

The better-class Icelanders, who become infected away from home, are accustomed to lead a quiet, uneventful life; they submit themselves to proper treatment, and do not marry until after the expiry of the prescribed time, so that they are not likely to propagate the disease.

As to strangers, they encounter many difficulties in their attempts to reach Icelandic women.

I fully agree with the opinions of Dr. Schierbeck. During my residence in Iceland my attention was specially directed to the present existence and the history of the first appearance of syphilis, and I am now able to put before you the result of my investigations. As Schierbeck's observations have shown, the people of Iceland are not immune to syphilis. I can recall at least two Icelanders in the employment of Mr. Haslund who were under treatment during the time that I was *chef de clinique;* and I have recently had under direct observation in Iceland two cases of syphilis, one of which was contracted in Copenhagen, and the other after marriage in Iceland.

The disease has several times spread in the form of small epidemics throughout the island.

In the "Annales de l'Islande" for the year 1528* I find the following note:—

"During this time there prevailed a widespread epidemic, which was called *Sárasótt* (ulcerative disease). It was of long

* Schleisner: Island undersegt fra at laegevidenskabeligt Synspunkt. Copenhagen, 1849, p. 51.

duration, and was both dangerous and very difficult to cure. There was then a German doctor called Lazarus Matthoenssen, surnamed Lassi, to whom it was agreed to hand over the farm of Skáneya, on condition that he undertook to cure *gratis* one hundred poor men who were tormented with the prevalent disease. Lassi went to the south of the country and took up his residence at Skáneya, but he only cured fifty of the poor patients, and entered into a dispute concerning half the land which had been given him."

In the biography of the first Medical Inspector-in-Chief of the island, Bjarne Povelsen, written by his son, use is made of this same word *Sárasótt* (p. 48) to describe the epidemic which prevailed in 1756 in the new wool factory at Reikiavik.

We know for a certainty that this epidemic was syphilis. The disease was imported by some French workmen in the wool factory, which in consequence afterwards became known in the songs of the Icelanders as *la fabrique de Frantzos.* The epidemic persisted till 1763, and even as late as 1774 a few sporadic cases were reported, but after that date nothing further was heard of it. In 1824 syphilis was again imported to the northern part of the country by some Danish sailors,* and the local doctor had during that year seventeen, and during the following year five, specific cases to deal with, almost all of them being derived from the population of two farms to which the epidemic confined itself.

Dr. Zenthen, of Eskifjord, has informed me that when he first arrived at Eskifjord in 1859 he found several families suffering from syphilis, which had been communicated to them by French fishermen. He immediately instituted the following energetic measures:—1, he forbade communication with foreign ships; 2, he inspected medically all persons on board such vessels; and 3, he suitably treated all those whom he found suffering from the disease. The epidemic was rapidly arrested, and its termination was hastened by the emigration of a large number of the persons already infected to North America.

In my opinion the reason of the limitation of the syphilitic attacks was to be found not so much in the pure habits of the population, which I believe to be neither better nor worse than those of other countries, as in the isolation of the patients, which

* Schleisner, loc. cit.

occurred as the necessary result of the conditions of Icelandic life. A disease like syphilis, which is a direct consequence of personal communication, can never penetrate deeply into the population of Iceland. It may cause familial epidemics. It would be improper for me to discuss the means necessary to prevent the spread of contagion to all the inhabitants of a farm, but if even one person has become infected it is easy to understand how the disease may spread to a neighbouring farm, *i.e.*, to a farm situated comparatively near as distances count in Iceland, because it is difficult to form an accurate conception of the long stretches which separate one human habitation from another in this island, but it is not likely to travel further.

Nor do I believe that it is correct to represent the Icelanders as a nation of peculiarly clean habits. It suffices to have seen and smelt an Icelandic dormitory in which from fourteen to sixteen people, men, women, and children, sleep together in six or eight huge wooden chests, to at once rid oneself of such misleading theories.

One finds, besides, in their popular books on medicine abundant evidence that the Icelanders as a race possess ordinary human instincts, which are accentuated rather than minimised by the solitude, the long winter evenings, the cold, and the lack of other occupation. It is moreover a suggestive fact that the penis is popularly called "*halfviur*."

I will now quote to you some of the curious domestic and erotic remedies which are found described in the popular medical literature of Iceland.

If a husband desires to make sure that his wife will love him and him alone, he must cut off a lock of her hair, burn it, and sprinkle the ashes upon his penis, thereafter rubbing them well in with honey. He must then go to bed with her, and she will never again be disposed to cohabit with others. Should he desire subsequently to destroy the enchantment, which might become irksome, he must then cut off a lock of his own hair and proceed similarly.

If a wife is not responsive to the attentions of her husband, he must procure some of the fat of a medium-sized he goat and anoint his penis before coitus, or he must take some goat's bile or fat, have it thoroughly dried, powdered, and mixed with warm clear oil, this is to be used as an inunction to the penis under

similar circumstances; thereafter the wife will never desire to desert her husband for strangers.

If a husband wishes to be assured of the chastity of his wife, all he requires to do is to place a magnet under her pillow; if she is chaste, she will turn towards her husband and embrace him; but if she has been unfaithful to him she will turn away and will fall out of bed as though she had been forcibly dragged therefrom.

If Icelanders have never known any better means than this of proving adultery, it is easy to understand how the population has acquired a reputation for modesty as well as for habits of purity.

If one desires to know whether a certain woman is a virgin or not, it is only necessary to powder a small quantity of agate as fine as possible, and to give it her to drink in some water or wine. If she is not a virgin, she will at once find it necessary to micturate, but if she is, she will have no difficulty in holding her water.

If a woman wishes to frustrate the discovery that she has lost her "greatest treasure," she must thoroughly moisten an oak gall-nut, and use it as a local application to the interior of her genitals, or, that failing, she must anoint them with saltpetre and honey.

The innumerable domestic remedies of this kind are certainly not evidences of the prevalence of a temperament such as belonged to Joseph or Saint Anthony.

The time, of which Arngrimur Jonssen* speaks, is long since past when the violation of a free-born girl was punished by death; when a kiss given to a virgin against her will, or the violation of a feud woman, was punished with exile; and when a kiss given to a virgin with her full consent, or the violation of a slave, was punished by a fine of three marks silver.

At the present day, the Icelanders embrace one another as a matter of ordinary salutation; they kiss one another when they meet, and embrace before they part, but it does not nowadays cost three marks; on the contrary, the custom is so common that there is difficulty in avoiding it.

Formerly the population were given to reunions, at which dancing and singing took place, and which were known under

* Crymogœa, p. 89 (quoted from Schleisner).

the name of "Joies," and they also occasionally held large fêtes called "Vikivikar." Sometimes these rejoicings would seem to have been full enough of animation, for at the commencement of the eighteenth century,* the bailiff of the under-prefect Vidalin forbade the holding of a "Joie" at the farm of Jaerva, because he calculated that nineteen children had resulted from the last similar festive occasion.

My attention has been also directed to the existence of general paralysis in Iceland. Syphilis being a rare exception, general paralysis ought to be still more rare if there is any relationship between these two diseases.

It goes without saying that, personally, I am convinced that general paralysis is due exclusively to syphilis, but there still exist certain persons, whose faith in this relationship being weak, are none the worse of having it fortified.

Mental diseases are quite as frequent in Iceland as in Denmark, indeed Finsen† believes them to be even more prevalent, and this fact has been confirmed by each of the eighteen doctors (the island possesses thirty altogether) with whom I have had occasion to discuss the question.

Each one of them replied to my first question as to whether nowadays syphilis was in reality so rare in Iceland, that they practically never met with the disease except among the inhabitants who had contracted it abroad, or among the foreign sailors who did not find much opportunity for spreading it, because sexual intercourse is of rare occurrence between them and the native women.

At Dynefjord only (on the west coast) where there is one whale and several cod fisheries, and where consequently foreign sailors are more abundant, cases of syphilis are met with.

Dr. Sigurdur Magnusson has informed me that in 1893 he had a small familial epidemic implicating three persons; the wife infected by a sailor, the husband by his wife, and a child by the parents. We have also visited in this place certain huts called by the people "le Bordel" and "le Convent des nonnes," designations which are none too flattering to the morality of the inhabitants. Before one of these huts we found a handsome little boy playing; he had black hair and eyes, and was unmis-

* Stephenson, "Iceland in the Eighteenth Century." Copenhagen, 1808.
† Sygdomsforholdene; Island. Copenhagen, 1874.

takably French in type, while the doctor told us that inside the house there was another child as unmistakably American, who was born of the same mother. Before another hut an old hemiplegic walked with difficulty, supported by a stick; striking evidences of the fecundity and disease which were alike possible to ensue from too intimate association with foreign sailors.

My second question addressed to these doctors, whether they ever encountered general paralysis, was answered in the negative by all except one man, Dr. Oddur Jonsson, who had practised medicine on the same fjord for upwards of eight years. He declared that during these eight years he had met with two cases of general paralysis, one of which was dead but the other still survived. He was unaware whether either of the two patients had suffered from syphilis, but they both *lived in huts whose female inmates had been associated with foreign sailors.* I may add that the other Icelandic doctors all affirmed that they believed themselves capable of recognising general paralysis, if it came before them, the pathological picture in a well-developed case being sufficiently typical to prevent error.

Conclusions.—First, the Icelanders are far from being immune to syphilis, but the disease is rare in the island and does not spread throughout the population. Its introduction is not safeguarded by the habits of the people so much as by the necessary isolation imposed by nature on the inhabitants of this barren island.

Second, general paralysis has been observed once only in the capital of the country, and then in a man who for six years had lived a somewhat fast life abroad; and perhaps twice in the only port of Iceland where there are some members of the native population who accept the advances of foreign sailors, and who have occasionally been infected by them.

General paralysis is unknown throughout the rest of the island.

RECURRING SYPHILITIC ROSEOLAS.

BY

PROFESSOR ALFRED FOURNIER.

Extract from the Chronicles of Dermatology and Syphilography, October, 1896.

TRANSLATED

BY

DR. GUTHRIE RANKIN.

RECURRING SYPHILITIC ROSEOLAS.

By Professor Alfred Fournier.

It has been for long fully recognised that syphilitic roseola is subject to relapses, in proof of which the name of recurrent roseola has been given to one of the eruptive varieties of the disease. But what is not nearly so well known is the fact that, on the one hand, roseola may relapse a whole series of times, even as many as four, five, six, or seven, examples of which I will bring before you; and on the other, that these relapses can take place at long intervals from the beginning of the disease, being met with in the course of the fourth, fifth, or sixth year, or even later. It is, of course, not rare for syphilis to manifest itself by the repetition of a single phenomenon at short intervals of time; but what, though no less characteristic, does not enter into the usual order of things, is to see the disease (except in its tertiary stage) confine its successive manifestations over widely separated periods to the same eruptive type.

Ricord himself has compared syphilis to an evolution—"a long, many-coloured ribbon which unwinds itself, and of which the tints vary after a certain number of turns, without the colour of one piece ever recalling that of those which have preceded it." This picturesque comparison pourtrays very happily the evolution of the disease as a whole, and in its broad features, but it is none the less faulty upon some points of secondary importance. This is the case as regards the subject of this paper, because we are about to consider a singular manifestation of syphilis which finds expression in the same morbid type at intervals of several years distance from one another. The morbid type referred to is *Roseola*, which is probably one of the earliest phenomena of the disease, occurring usually at the very commencement of the secondary period, properly considered by everyone as the prototype of secondary manifestations; but which, as a curious exception, sometimes subsides only to appear again during the period of the disease which is chronologically

tertiary, that is to say, four, five, six, if not even more, years after the date of infection.

The two points to which I propose in this paper to direct special attention are, (1) the possible multiplicity of the relapses of roseola; and (2) the singularly long intervals which may elapse between these recurrent roseolar storms.

I owe my knowledge of these two points exclusively to my private practice. Indeed they are related to certain clinical details which, for the two following reasons, are hardly ever met with at an hospital. First, only exceptionally is it possible to keep hospital patients under observation throughout a long series of years; and second, the nature of the symptoms is such that patients seldom resort to an hospital for their treatment. A workman, or employé, who earns his living by daily toil, will not lose a day's wage in order to come to one of our cliniques to show us some cutaneous spots which give him no discomfort, which are not of such a character as to alarm him, and which, indeed, he has hardly given any attention to. On the other hand, a man of the world, whose time is his own, who is more particular in the care of his person, and who does not grudge the cost of a consultation, will never fail to come to his doctor for advice concerning such blotches.

I.

Those roseolas which are subject to repeated relapses have been called attention to and studied by many authors, notably by Ricord, Bancreau, Cullerier, Bazin, Hardy, Pillon, Vidal, Besnier, &c., while I have already elsewhere fully described them. My sole aim now is to complete their history as regards several details which have been heretofore obscure; more particularly the multiplicity of their recurrences, which is often surprising; the intervals which separate them, which are frequently of long duration; and their relationship to another variety of roseolar exanthem of slow development, to which I think the name of *tertiary erythema* ought to be given.

I. Let me say at once that these eruptive types are not rare. I have notes of more than a hundred cases met with in private practice, and can remember many more.

II. In the second place, the analysis of 32 cases (the only ones

to which I will refer in this paper, because unfortunately my notes of the others are neither detailed nor complete) furnishes me with the following figures bearing upon the number of relapses which are possible in these exanthems :—

5	cases	in	which	the	roseolar	exanthem	recurred 2 times.
7	,,	,,	,,	,,	,,	3	,,
4	,,	,,	,,	,,	,,	4	,,
8	,,	,,	,,	,,	,,	5	,,
5	,,	,,	,,	,,	,,	6	,,
2	,,	,,	,,	,,	,,	7	,,
1	,,	,,	,,	,,	,,	8	,,

It is impossible, though it must be more fully referred to later on, not to be struck, in passing, by this curious fact, that in the same patient there may be five, six, seven, or eight outbreaks of a roseolar exanthem. The possibility of such recurrences has not been widely recognised up to the present time.

III. In the third place, at what intervals are these successive attacks of the roseolar exanthem produced? Making allowance for the initial eruption (which for the moment need not be considered), investigation of the cases in question brings out the following results :—

In the course of the	1st	year	...	...	...	...	33 times.
,,	2nd	,,	...	...	...	...	41 ,,
,,	3rd	,,	...	...	...	...	18 ,,
,,	4th	,,	...	...	...	...	9 ,,
,,	5th	,,	...	...	...	...	5 ,,
,,	6th	,,	...	...	...	...	3 ,,
,,	10th	,,	...	...	...	...	1 ,,
,,	11th	,,	...	...	...	...	1 ,,

Again, is it not a most surprising fact that a purely roseolar exanthem should make its appearance at intervals so far removed from the normal incidence of such a rash as the fourth, fifth, or sixth year after infection, without even taking into account the two cases noted last in the list, where I believed I observed the roseola in the tenth and eleventh years after the illness? (On account of the exceptional and altogether extraordinary character of these two cases, they may, in order to avoid the possibility of error, be in the meantime provisionally set aside.)

From this first analysis the following conclusions may be arrived at :—

1st. That certain eruptions of an erythematous type (com-

monly called roseolas) may be produced in syphilitic patients for a succession of five, six, seven, or eight times.

2nd. That these eruptions, which are purely erythematous, have been, with certainty, observed up till the sixth year of syphilis, and perhaps even at later dates.

IV. To these first results let me add, in order to complete the general idea of the subject, the following two considerations:—

1st. These recurrent roseolar exanthems are almost exclusively confined to patients who have been subjected to treatment, and sometimes to those who have been treated correctly throughout a long period of time.

In short, all the histories which I have gone into for the purposes of this paper are concerned (with one exception) with patients who have been treated by mercury, the greater number having pursued active treatment for an average period, but some having submitted themselves to a course lasting throughout several years.

With some reason, then, one can say of these exanthems that they are "roseolas modified by mercury," not necessarily that mercury can be made responsible for these roseolas and their recurrences, but that it apparently exerts such a modifying influence upon syphilis that the virus becomes attenuated and the future manifestations of the disease are confined to the simplest and most superficial skin eruptions.

2nd. The character of recurrence enters so much into the spirit (I had almost said the humour) of this type of exanthems that a relapse having once occurred, another may, with almost unfailing certainty, be looked for within a short time. *One recurrent roseola is never long in being followed by another.* The patient's attention soon becomes fixed upon this point, and many times I have heard one or other of my clients say, "It is always the same thing, doctor; you will soon cure my new roseola, but you will see that very shortly I will be again attacked by it;" and as a rule their prognostications have come true.

II.

In confirmation of what I have already said, I will now direct your attention to some of my cases. I will not quote any where the erythematous eruptions in question have only

occurred three or four times, because such cases are so common as only to require mention. I will only place on record here certain others which have been strikingly remarkable from the excessive number of their relapses, and will limit myself to cases where roseolar exanthems have appeared upon the scene five, six, seven, or eight times.

CASE I.—*Syphilis; five roseolas in the course of the first two years.*

Z—, aged 35 years. Habitual good health; temperament slightly lymphatic. No history of previous skin eruption. Syphilis contracted in August, 1887. Indurated chancre with enlarged glands in both inguinal regions. Roseola of the usual type about the 24th of September. Treatment by the green iodide of mercury (two pills of 5 centigrammes each day) continued till the 15th November. Second course of treatment, comprising ninety-five pills, from December to February, 1888.

In September, October, and November, frequently recurring syphilides on the buccal mucous membrane (a smoker).

On April 7th, 1888, *a second eruption of roseola.* This presents the same dermatological characters as the first, but is much less confluent. "It is not," says the patient, "as regards the number of spots, more than one quarter of the first eruption." Third course of treatment by the green iodide of mercury (eighty-five pills). In addition, during August, treatment at Luchon by mercurial inunction.

Nevertheless, towards the 29th October, *a third roseolar eruption*, which declares itself in a very modified form. It is comprised by about twenty rose-coloured spots scattered here and there over the trunk of the body. They are about as large as a finger-nail, irregularly rounded, non-squamous, and are not irritable. There is no doubt as to their syphilitic character. On resuming treatment by the iodide of mercury, the eruption disappears in eight days.

On the 2nd February, 1889, the patient, who was very observant of himself and very anxious as to his condition, comes to show me two spots which have come out upon his chest. Purposely I refrain from treatment and await developments.

By the 8th February the spots are increased in number, and I am able to count a dozen. They are absolutely identical with

those of the previous eruption and are beyond doubt specific. Against my wish, the patient at once resumes mercurial medication, which he perseveres with till the 31st March. Ever since the 20th February, entire disappearance of this *fourth eruption.*

On June 8th, *a fifth eruption.* About ten spots, all of them similar to those of the preceding eruptions. No treatment. By the 19th the eruption has become somewhat more abundant, and the spots now number about thirty. Dupuytren's pills, at first two, later on three a day. Disappearance of the eruption about the 10th July. Subsequent treatment by alternate methods (mercurial inunction, Dupuytren's pills, iodide of potassium). Absence of any fresh symptom up to the present time (October, 1896).

CASE II.—*Syphilis; five (or perhaps six) roseolas between the first and third years. No other specific manifestation.*

N—, aged 42 years. Strong constitution. No important morbid antecedents.

In August, 1893, indurated chancre of the penis. No internal treatment.

October 9th.—Roseola of ordinary character and of moderate confluence. Treatment: two pills of green iodide of mercury containing each 5 centigrammes. The patient takes one hundred of these pills. A second course of treatment comprising eighty pills, from January to April, 1894.

On the 28th, the patient comes to show me some red spots which had appeared the preceding day. These spots appear to me to be a *return of roseola,* but I am unable to be positive in my assertion as to their nature. Another course of treatment to the extent of eighty pills.

May 2nd, 1895.—A typical eruption of *roseola.* This second (or perhaps third) eruption is much less confluent than the first. It occupies the trunk exclusively. Renewal of treatment by Gibert's syrup.

November 9th.—A third roseola, which is round, or circinate in form. It is composed of about ten rings of a very delicate pale rose colour. Some are plainly visible, but others are ill-defined and require some looking for, because on account of

their extremely pale colour they do not catch the eye at first sight. Renewed treatment. The spots disappear almost immediately. An attack of gonorrhœa necessitates interruption of the treatment.

December 18th.—A fourth roseola of circinate form, and distinctly more intense than the former. At least twenty rings can be counted; they are circular or oval, with erythematous margins surrounding healthy skin, though some have their central portion lightly rose-coloured, with a margin of brighter tone. Pills of green iodide of mercury. Treatment stopped after taking twenty pills on account of a slight passing indisposition.

July 4th, 1898.—*A fifth roseola* of a week's duration. This is a mixed form of eruption; here and there are some spots of an oval or discoid shape, and of the size of an almond or 20-centime piece; elsewhere small ring-shaped or oval spots of undecided outline, mixed with others of similar shape whose centres are slightly erythematous. I prescribe injections of calomel for this patient. He seems so afraid of this suggestion as to treatment that he says to me, "The pills of iodide of mercury have always hitherto cleared these spots away in four or five days." Not seen again.

CASE III.—*Syphilis; six roseolas in the course of the first three years after infection.*

B—, aged 28 years. A healthy-looking person, without any important morbid antecedents.

Contracted syphilis towards the end of August, 1887. Perineal chancre, with enlargement of inguinal glands on the left side. No general treatment.

October 14th.—Roseola of the usual type and of a moderate degree of confluence. Treatment by pills of iodide of mercury, 5 centigrammes in each; two pills per diem.

In November and December, mucous patches on the tonsils. Fresh patches on the tongue and throat in February, 1888. The occurrence of gonorrhœa compels temporary cessation of treatment.

February 25th.—A second roseola, less intense than the first. In addition, erosive syphilides of the tongue and palate.

Return to specific treatment.

In March and June, fresh buccal syphilides.

In September, *a third eruption of roseola.*

December 24th.—A fourth eruption, in spite of the patient having already swallowed 390 pills of iodide of mercury. This rash is comparatively insignificant as regards the number of spots, which are moreover very pale, and many are only to be made out at all by careful examination. It is necessary, indeed, as the patient himself says, "to look for them to see them." Resumption of treatment. Disappearance of the spots after the 31st December.

March 29th, 1889.—*A fifth development of roseolar spots.* The eruption is practically identical with the preceding one. Two of Dupuytren's pills daily. Disappearance of the rash on the twelfth day.

In August, treatment at Uriage by mercurial inunction; subsequently iodide of potassium.

Nevertheless in February, 1890, *a sixth measly eruption*, consisting of a dozen red spots on the thorax. These spots are irregularly rounded, and are of the size of a 50-centime piece; they are pale and not squamous. Renewal of treatment by Dupuytren's pills, followed by iodide of potassium.

In April, 1891, a palmar syphilide. Hypodermic injections of the peptonate of mercury, followed by mercurial inunction at Luchon.

Again in June, 1892, a circular papulo-squamous syphilide of the scrotum. Injections of calomel.

In February, 1893, double specific epididymitis. Treatment by iodine and subsequent injections of calomel. No new development up till now (October, 1896).

CASE IV.—*Syphilis; six roseolas, five of them circinate in the course of the first three years after infection.*

E—, aged 22 years. Temperament slightly lymphatic. Arthritic tendencies. Early alopecia. Varicose veins. Mother the subject of gravel and of "rheumatic gout." Hard chancre in May, 1879. In July, *papulo-erythematous syphilide;* angina; headaches; alopecia; enlargement of posterior cervical glands. Subsequently mucous plaques on the tongue and tonsils. Treatment by pills of the green iodide of mercury.

December 22nd.—Lingual syphilides and *annular roseola*. I prescribe a renewal of the pills, but this treatment being badly borne, the patient substitutes Gibert's syrup, recommended to him by his doctor. Very rapid disappearance of the eruption.

April 13th.—A third roseola, annular in form and fairly discrete. Lingual syphilides. Treatment for one month by Gibert's syrup.

In June, buccal syphilides, which recur every month till 1881. Patient continues the use of Gibert's syrup, declaring that it is "the only mercurial remedy which his system will tolerate." Treatment otherwise followed very irregularly.

November 25th, 1881.—*A fourth roseola*, of circinate form. It is composed of circles or ovals of very unequal dimensions, some as small as an almond or 50-centime piece, others measuring in their greatest diameter as much as four or five centimetres. Pills of the green iodide of mercury.

April 11th, 1882.—The patient, who is away from Paris, informs me by letter that he has just discovered *a fifth roseola*, ring-shaped, and in all respects resembling that of November. The same treatment.

September 30th.—A sixth roseola of annular type. Curious particularity; some rings or ovals, measuring across their greatest diameter four or five centimetres, present at their middle a small, well-developed, erythematous patch the size of a lentil or 20-centime piece. This is so clearly marked that each eruptive patch seems to be made up of three concentric zones, one external and erythematous, another intermediate and composed of normal integument, and a third or central, again erythematous (Cockade roseola). One of my esteemed colleagues, called in consultation, expresses the opinion that the eruption might possibly be an "arthritic erythema." In accordance with this hypothesis the patient is treated with alkalies.

The eruption persists, *without modification*, till the 15th November, in spite of this treatment. The patient becomes fretful at his slow progress and resorts again to the iodide of mercury pills. The eruption disappears "*in less than a week.*" Several courses of treatment by green iodide of mercury and iodide of potassium.

No further development.

CASE V.—*Syphilis; six roseolas (of which five are circinate in type) during the course of the first six years of the disease.*

E—, 25 years of age. Constitution not too robust. Indurated chancre on the penis in February, 1874. *Roseola* of the ordinary type. Buccal mucous patches recurring frequently. Treatment conducted by Dr. Simonet (300 pills of sublimate, several litres of Gibert's syrup), more recently 100 Dupuytren's pills.

In July, 1875, *circinate roseola* in the form of irregularly shaped crowns or ovals, with curiously festooned or lanciniated margins. The crowns are about the size of a two-franc piece, and the ovals have their largest diameters varying from two to three centimetres. Treatment by iodide of mercury pills. Frequently recurring buccal ulcerations produced by the excessive use of cigarettes. Ultimately iodide of potassium. Alopecia, anæmia, emaciation.

In July, 1876, *a third roseola*, approximately analogous in character to the preceding outbreak. Resumption of the iodide of mercury pills. Tonics of quinine and iron. The patient has become subject, since the onset of his syphilis, to frequent attacks of herpes.

In June, 1877, *a fourth roseola*, of circinate type. This roseola is exceedingly pale in colour, and can only be discovered by careful observation. Treatment by iodide of mercury to be resumed for three or four weeks. Very rapid disappearance of the rash. Treatment at Luchon in 1877, and at Uriage in 1878.

In July, 1878, *a fifth roseola*, again circinate in character. Return to the same treatment, which the patient gives up, after two or three weeks, as soon as the eruption has vanished.

In May, 1879, *a sixth roseola*, circinate in type. Iodide of potassium. Treatment at Luchon.

In 1880 and 1882, lingual syphilides. Since then, no further manifestation.

CASE VI.—*Syphilis; seven eruptions of an erythematous syphilide during the course of the first five years of the disease. Annular syphilide in the form of a single ring.*

Madam H—, aged 31 years. Habitual good health. Nervous temperament. Syphilis contracted from her husband in March, 1890.

In April, *roseola*, with violent neuralgic pains in the head and jaws. Treatment by pills of green iodide of mercury, together with quinine and iron tonics.

In July, syphilitic manifestations on the tonsils.

In November, *a second roseola*, which is markedly discrete, and consists only of about twenty spots scattered over the thorax and abdomen. Treatment resumed.

In June, 1891, *a third roseola*, again discrete, perhaps even more so than the second. Treatment again resumed, but not continued longer than three weeks. Disappearance of the spots "in a few days."

In July, *a fourth roseola*, comprising no more than a dozen erythematous spots. Labial syphilides. Treatment resumed, but only intermittently carried on because of the occurrence of dyspepsia and diarrhœa.

In October, *a fifth roseola*, exceedingly discrete and similar to the previous attacks; disappearing entirely after the use of a few pills.

In April, 1892, *a sixth roseola*, of circinate type, and comprising about ten annular or oval erythematous spots, non-squamous, and of a delicate rose colour. More alarmed by this eruption than by any of those which preceded it, the patient resolves "to submit at last to continuous treatment." I prescribe mercurial inunctions, eight of which suffice to dissipate the rash, after which treatment is again suspended.

In July, one spot in the palm, characteristically specific. Treatment at Uriage; twenty-five mercurial inunctions. After this course of treatment, no manifestation during 18 months.

In December, 1892, bone pains, specially referred to the left humerus. Iodide of potassium.

In July, 1894, *annular syphilide*, showing itself in the form of a single ring, but absolutely typical and unmistakable. This ring appears on the thigh; it is a complete circle, exclusively erythematous, and without subjacent infiltration or mixture with squamous elements. Mercurial inunctions. Disappearance of the rash after one week's treatment.

In April, inunctions are resumed. Nevertheless, in May, a fresh occurrence of bone pains, which are rapidly alleviated, and finally cured, by iodide of potassium. No further manifestation up to the present time (October, 1896).

CASE VII.—*Syphilis; seven annular roseolas between the fourth and eleventh years.*

N—, aged 19 years. A person who is not strong, is thin, and subject to frequent attacks of bronchitis. A sister is threatened with tuberculosis.

Contracted syphilis at the age of 19, in July, 1868. Four chancres on the penis, which, having been looked upon at first as simple sores, were not recognised as specific until a comparatively late period. He was put under treatment as soon as the true nature of his ailment was recognised, and declares that in 1868 and 1869 he took 260 pills of 5 centigrammes each of the green iodide of mercury, and about 700 grammes of Van Swieten's liquor. He experienced only very slight secondary symptoms, which were confined to recurrent mucous plaques in the mouth (he is a smoker) and a few occasional disseminated papules scattered over the body. In 1870 and 1871 he underwent several courses of treatment by iodide of potassium.

In December, 1871, lingual mucous plaques, crusted syphilide of the scrotum, and *annular roseola* of the trunk, of a markedly discrete variety. Mercurial pills for about a fortnight. Disappearance of all symptoms. Iodide of potassium. Shortly afterwards a papulo-circinate syphilide of the scrotum.

In June, 1872, *a second eruption of annular roseola.* Half a dozen erythematous rings, the greater number of which are as large as five-franc pieces. Gibert's syrup. Very rapid disappearance of the spots.

Recurrence in September of another *annular roseola*, the individual spots of which are of such a delicate rose-tint that they are not readily seen. The same treatment. The spots disappear almost at once.

In January, *a fourth annular roseola.* A dozen pale rose-coloured rings, two of which are in contact and closely resemble the figure 8. It is worthy of note that in this eruption the rings are small, and do not exceed in diameter the size of a fifty-centime piece. Pills of iodide of mercury. The spots disappear in a few days.

In March, *a fifth annular roseola*, composed of only a very few rings. Twenty iodide of mercury pills chase away the eruption. Subsequently iodide of potassium and Gibert's syrup.

In July, 1875, *a sixth circular roseola*, comprising a dozen rings on the trunk and two upon one leg. The eruption possesses the same characters as its two immediate predecessors.

In April, 1879, *a seventh circular roseola*, still more scattered than the preceding.

This patient, except at the commencement of the illness, has never allowed himself to be treated continuously and thoroughly, but only, according to his own expression, "by fits and starts." As soon as symptoms developed, he came to see me in a state of great alarm, followed the prescribed course of treatment for some weeks, and gave it up as soon as the symptoms had disappeared. His case is an example of the unsatisfactory results attending opportunist treatment.

Periodically he has been the subject of various specific manifestations, the most serious of which was a pulmonary gumma which he developed in 1886. About this time, prolonged and active treatment. Since then, till 1896, no fresh manifestation.

CASE VIII.—*Syphilis; eight roseolas during the currency of the first four years after infection.*

R—, aged 28 years. Habitual good health. Temperament slightly lymphatic.

Indurated chancre of the penis in June, 1893, with specific adenitis.

Treatment during two months by green iodide of mercury in doses averaging 8 centigrammes daily.

In October, tonsillar syphilides. Treatment resumed.

In November, *roseolar eruption*, very scattered, which disappears in a few days under the influence of treatment. In spite of the resumption of treatment in November, on the 4th of May the patient again comes to show me a *roseolar eruption*, consisting of about ten spots sparsely scattered over the thorax, of a pale rose colour, fairly large, and non-squamous. Treatment again resorted to. The rash disappears in a few days. Treatment suspended in June.

August 7th.—A third roseolar eruption, in every way similar to the preceding. Headache. Renewal of mercurial treatment. Rapid disappearance of all symptoms.

October 26th.—Treatment has been continued since 6th

September, but nevertheless, within the past few days, there has been a recurrence of a widely-scattered *roseolar eruption*, consisting of about fifteen pale rose-coloured spots spread over the chest and limbs. Pills of iodide of mercury. The rash disappears in less than a week.

May, 1895.—*A fifth roseolar eruption*, exactly resembling its predecessors, consisting, that is to say, of about a dozen exceedingly delicate rose spots as large as a 50-centime piece, neither pruriginous nor squamous, irregularly orbicular, and chequered at the circumference. As usual, specific treatment dissipates this eruption in less than a week. A tenth mercurial course of iodide of mercury to the extent of 10 centigrammes per diem for six weeks is undertaken in October.

This notwithstanding, on the 26th December there is a return of the *roseolar eruption*, identical with its predecessors, and consisting of upwards of twenty spots disseminated over the chest.

A *seventh eruption* of like nature appears in May, 1896, and is comprised in half a dozen spots situated on the thorax. Purposely I refrain from treatment. The eruption persists for some weeks before it disappears.

Finally, on the 6th of July there is an outbreak of an *eighth eruption* of a new and more important character. It consists of about twenty spots of *annular roseola*, irregularly oval in shape, with broken borders surrounding healthy skin, and measuring from 1½ to 2 centimetres in their greatest axis. They are rose-coloured, but of a very pale tint, so that they do not at once catch the eye, indeed some of the rings are only appreciable in a favourable light, and after careful examination. The specific character of this exanthem is not to be doubted for a moment.

Treatment at Uriage by mercurial inunctions. No new morbid development up to this date (October, 1896).

III.

Under what conditions do these recurrent roseolar exanthems manifest themselves?

I. It would be an absolute error to represent a recurrent roseola as the necessary reproduction of a primary roseola, such, for example, as commonly accompanies the onset of the

secondary stage of syphilis. Almost invariably, on the contrary, the secondary roseola is only a *diminutive*, most frequently indeed a diminutive very much diminished (if I may be permitted to thus combine two synonymous words) of that ordinary form of roseola which everyone knows, and which I need not stop to describe here.

To be more precise, it is, in the first place, exceedingly rare for a second eruption of roseola to perfectly reproduce a first. It may be, again, tolerably bright, or even fairly confluent (and of this I have recently seen an example), but almost always, even in the case to which I refer, it is differentiated from the first by a lessened eruptive importance. I mean that it is, on the one hand, *less widespread in distribution*, or, on the other, less confluent, *less rich in the number of its individual eruptive elements*. It is, relatively to the eruption which preceded it, a roseola which is more circumscribed and, at the same time, more feeble and delicate.

In the second place, and more importantly, the common experience—what one may call the rule—is that this attenuation of recurrent roseolas, from the double point of view of their area of distribution and of the number of their spots, is accentuated in a very marked degree in the later eruptions—the third, fourth, sixth, &c.—and often even as early as the second.

This attenuation may reach *all possible degrees*, so that it would be superfluous to write of it in detail.

It begins by producing roseolas which are circumscribed and discrete, and which, in amount, do not represent more—if I may be pardoned stating it in this way—than the third, fourth, or sixth part of a roseola of the usual type, looked at from the point of view of comparison.

Moreover, by a series of successive attenuations, these roseolas ultimately end, first, in no longer occupying more than an extremely restricted territory; and second, in comprising a distinctly lessened number of eruptive elements, amounting to no more than 100, 50, 30, &c.

Eventually these elements may be reduced—and such an occurrence is by no means rare—to a minimum number of spots, as, for example, in many of the cases previously detailed, in which twenty, fifteen, a dozen, or even half-a-dozen rose spots comprised the entirety of the roseolar manifestation.

When they reach this minimum, they become diagnostically unrecognisable, and if, between them and the ordinary type, one did not meet with all kinds of intermediate modifications, it would hardly be permissible to label such singularly attenuated eruptive conditions as "roseolar" at all.

Occasionally these roseolas present themselves in such an unostentatious form that they are represented by a solitary eruptive element, as in Case VI.

As to situation, recurrent roseolas are most frequently met with on the chest, and particularly on its lateral aspects—less often on the flanks or the buttocks, more rarely still on the limbs (the bulge of the shoulder, the anterior aspect of the forearms, thighs, &c.). Their few spots may also be simultaneously distributed over several situations, such as the trunk, the flanks, and the limbs.

II. So far as dermatological characters are concerned, they are, from every point of view, true roseolas. Like common roseola, indeed, they consist of simple unraised cutaneous spots, which are not attended by thickening of tissue at their base, are rose-coloured, non-squamous, unaccompanied by aching, and disappear by natural resolution without leaving stains behind, &c.

They are not always exact imitations of common syphilitic roseola. They differ from it somewhat, and especially in the two following particulars.

1. Their spots are generally larger, more spread out than those of a primary roseola. On an average they are as large as a nail, that of the index-finger for example. They may even become so large as to be comparable to an almond, or sometimes to a prune or a one-franc piece; while exceptionally some are met with which cover a surface as large as a five-franc piece.

2. They are certainly of a less intense rose colour than ordinary roseola, and often they possess no more than a delicate, pale rose tint. So much so that, on account of this attenuation of tint, they are not always seen on a superficial inspection, and to be found, often require to be searched for by the aid of a bright and favourably situated light.

I may add that their contour is generally badly defined and seems to insensibly melt into the natural colour of the adjacent skin.

III. Finally, they not uncommonly assume an eruptive character special to themselves, namely, the circinate type, or, to speak more accurately, the annular or oval type, which is represented by erythematous rings or ovals enclosing healthy integument.

I may further explain that, in this form, the erythematous element, in place of constituting a disc or even surface such as would be produced by a drop of water falling on the ground, arranges itself in a circinate zone, rounded or oval, and thus forms a border to a segment of healthy skin. This rosaceous zone of two, three, or four millimetres in size forms either a complete oval (more often than a circle), or more frequently a broken oval, composed of two or three interrupted segments which convey to the eye the general impression of an oval, but delineate it only incompletely.

The oval thus produced is variable in its proportions, but as a rule its greatest diameter does not exceed from two to three or four centimetres.

This type of circinate roseola is fairly common, and is met with in about one-third of all cases (ten cases in thirty-two). In the large majority (seven times in ten) it is only *consecutive*, and is produced subsequently to roseolas of ordinary type.

The following examples are collected from my note-book :—

3 cases where one circinate roseola has succeeded one ordinary roseola.
1 case where three circinate roseolas have succeeded one ordinary roseola.
1 ,, two ,, ,, ,, four ,,
1 ,, five ,, ,, ,, one ,,
1 ,, three ,, ,, ,, two ordinary roseolas; to be followed themselves by a roseola of mixed type, having discoid or imperfectly circinate spots.

There are, however, some cases (three in ten) where successive roseolas never declare themselves except according to the circinate type. Case No. VII. is one of this description.

Evolution and duration.—Like all secondary manifestations, recurrent roseolas are capable of spontaneous resolution, but the process appears to be a slow one. I have had under observation several cases in which, according to the patient's story, the eruption had already been present for periods varying "from several weeks to two months and more." As a compensation, however, they yield rapidly to specific medication, those of circinate form, however, being sometimes slightly rebellious. In

from twelve to fifteen days at the most, mercury clears off the rash, and often accomplishes its purpose in as short a time as eight or ten days. In one of my clients, who had a right to call himself an expert in the matter, the multiple recurrent roseolas from which he had suffered were always dispersed "in four or five days" under the influence of pills containing iodide of mercury.

Ætiology.—One curious fact which has been elucidated, as I have already mentioned, is that recurrent roseolas are almost exclusively met with in patients who have been treated, and even in such as have been skilfully treated. One is therefore rather tempted to look upon them as expressions of syphilis not yet extinct, but attenuated by the treatment.

It is no longer a matter of doubt that they are not notably more common in men than in women.

Beyond this, we know nothing of their ætiology. What are the predisposing causes which specially conduce to these curious roseolar manifestations, which persistently recur, and always according to the same type—a type, moreover, which is out of harmony with the stage of the disease in which it is met with, *i.e.*, occurring under forms which are essentially secondary, whereas they ought to have acquired tertiary characteristics? This entirely baffles us.

It has been stated that these recurrent roseolas are more specially observed in arthritic subjects, and in such as are subject to herpes, seborrhœa, eczema, &c. My personal investigations do not confirm these assertions.

Prognosis.—It goes without saying that, by themselves, roseolas constitute only unimportant symptoms. But they carry with them an unfortunate prognostic value of another kind, from the moral effect which they produce. They are manifestations which, on account of their frequent recurrences, give rise, in certain patients, to impatience, unrest, discouragement, and even despair, because in the eyes of such persons they bear witness to an infection which is permanent, incurable, inaccessible to treatment, and destined to be everlasting.

Frequently I have heard certain of my clients who were thus afflicted express to me their misery and disappointment on this score by saying, "You see, doctor, we will never come to an end of this terrible syphilis. I have done everything you have told

me, I have drenched myself with mercury, yet these same manifestations go on recurring. Here I am with yet another roseola, which clearly proves to me that my cure is no further advanced than at the beginning of my illness four, five, or six years ago. I have lost my courage, and am broken-hearted."

Nevertheless these feelings of disquietude and misery are not justifiable. For one reason, we always get to the end of such symptoms by persistence in treatment; and for another, manifestations of this nature bear no serious prognostic significance either for the present or the future.

As to the present, the evidence they afford is obvious, because almost invariably these recurrent roseolas are strong indications of an actively benign form of syphilis, and are often the sole expression of the disease throughout many years.

And as to the future, it has never been shown that they constitute an unfavourable sign. So far as I know, they have not been observed in cases of syphilis with threatening tertiary manifestations, and in my own experience I can only find among my notes two cases where they have been followed by tertiary developments (exostosis in one case, and a pulmonary gumma in another). I am therefore disposed to look upon them as of favourable prognostic value, not, let it be understood, because of any virtue inherent in them, but on account of the continuance of treatment which the frequency of their recurrence demands.

Treatment.—The treatment of these recurrent roseolas is no different from that of every other specific disorder, which is specially rebellious and prone to relapse; that is to say, to become curative, it ought to be preventive throughout. The method of treatment known as opportunist, which consists in the use of remedies during the presence of the specific symptoms, and in the withdrawal of them as soon as these manifestations disappear, finds, in this class of case, its most striking condemnation; for from all experience, the only result attained by it is to allow these roseolas to acquire an increasing tendency to relapse. The preventive method, on the contrary, provides us with very different guarantees of success, and to it alone, empiric though it be, must recourse be had if a satisfactory result is to be attained. It must always consist in a series of courses of medication, separated from one another by intervals of longer or shorter duration according to circumstances.

One must not limit the treatment to the period of each relapse, but must persevere with it after the disappearance of symptoms for a sufficient length of time, even though there be an absence of any return of roseolar exanthem.

I believe that a succession of courses of specific treatment, carried on intermittently throughout two or three consecutive years from the date of the last eruption, is necessary in order to definitely cut short the peculiar tendency to recurrence of the roseolas in question, as well as to protect the patient from the future development of other manifestations.

Mercury is the drug which, from choice, must be relied upon, since iodine exercises upon the secondary stages of the disease only a mild and incomparably inferior influence. It should be administered in medium doses, as these will generally be found sufficient for the purpose; but in some cases it is necessary to resort to large and almost heroic doses in order to cope successfully with the more obstinate forms of recurring roseola.

It matters little, I believe, in what way the drug is given. Every method is successful, whether by inunctions, injections, or internal administration, provided only it is employed perseveringly. The essential point consists in the length of time during which a methodic and intermittent process of treatment is carried on.

IV.

Finally, is there an identity between the recurrent roseolar exanthems which I have described and these other roseolar exanthems which declare themselves at an advanced stage of syphilis, and to which I have given the name, now widely adopted, of *tertiary erythemas*?

One of my pupils, Dr. Brauman,* has made a very complete and interesting investigation into the nature of these erythemas. There are undoubtedly many and powerful arguments in favour of this identity. Tertiary erythema is, in short, from the dermatological point of view, nothing else than a true roseola unaccompanied by other eruptive elements—a roseola which is exempt from all subjective symptoms and notably from pruritus, a roseola which is frequently circinate like those which are

* "De l'érythème circiné tertiare de la syphilis," by Jules Brauman, Paris Thesis, 1891.

recurrent, a roseola which undergoes resolution, &c. Between it and a recurrent roseola objective diagnosis would be impossible in a large number of cases. Why then not make of these two types ordinary varieties of a morbid condition common to both?

On the other hand, however, the identity between them is not complete in every detail. In the first place, tertiary circinate erythema occurs, under special conditions, at long, and sometimes very long, intervals after the commencement of the disease (for example, 6, 8, 10, 13, 14 years or more from the date of the chancre), and also without being related to the initial roseola by a succession of intermediate roseolar eruptions. Dermatologically it is differentiated from the recurrent roseolas by two leading characteristics: first, a much smaller number of eruptive elements, and secondly by eruptive elements which are usually much larger (circles or ovals measuring 6, 8, 10, 15, or 16 centimetres in their greatest diameter). It has a shorter evolution, and is of considerably longer duration. Its tendency to recurrence is less. Lastly, and most important of all, it yields much less readily to specific treatment, to which it is often obstinately rebellious.

Are these reasons, however, sufficient to separate this eruptive type from the recurrent roseolas and elevate it to the dignity of a separate species? This is a question which is open to serious discussion.

The question still remains undecided. It requires further inquiry, and is worthy of renewed observations carried on in the direction which I have indicated in this paper. I content myself with stating it, without being at present in the position to supply a satisfactory answer.

ON PEMPHIGUS MALIGNUS

(WITH CLINICAL DEMONSTRATION).

BY

A. NEISSER, M.D.,

Professor of Dermatology in the University of Breslau.

TRANSLATED

BY

L. ELKIND, M.D.

ON PEMPHIGUS MALIGNUS

(WITH CLINICAL DEMONSTRATION).

By Professor NEISSER.

Gentlemen,

It was originally intended that my assistant, Dr. Westberg, should give you a detailed account of all the cases of pemphigus that have come under our observation, and a short sketch of the present state of knowledge with regard to the nature of pemphigus.

Our time, however, is so limited that I must confine myself to briefly introducing to your notice a patient who seems to me to be especially interesting.

The patient's case belongs to the class of pemphigus malignus. It is interesting for the reason that all the features, of which a single one usually suffices to mark cases of pemphigus as malignant, are found to exist together in him, and that, on the other hand, the course of the affection is more benign than we are accustomed to observe in patients afflicted with that disease.

As regards the *malignancy* of the case under consideration it consists of:—

1. *The primary appearance of the vesicular eruption on the mucous membrane.* The affection is said to have commenced in May, 1893, with a vesicular eruption on the lips. Three weeks later, after an attack of a violent burning feeling at night, there appeared on the following day vesicles which almost attained the size of a hen's egg. The eruption spread over the whole body. There was pain on deglutition, pointing to the fact that similar vesicles had developed on the mucous membrane of the pharynx.

The vesicles for the most part disappeared without leaving any traces; only on those parts which had been the seat of very frequent attacks there the skin remained thin and

atrophied, easily liable to form wrinkles, as we very frequently observe on the dorsum of the hands, on the shoulders, &c.

2. The second reason why the case must be looked upon as malignant pemphigus is furnished by the *tendency of the epithelium to desquamation*, which follows even the slightest traumatic pressure. Especially when the patient himself grasps anything tight, if while sitting in the bath he takes hold of the side to raise himself, or when we rub the skin lightly, it results in the detachment of *the epidermis and the uppermost epithelial layer*. Hence areas and streaks connected together, moist and secreting, are formed. Real vesicles are not present. In spite of this epidermolysis, which is typical of pemphigus foliaceus, the characteristic features of pemphigus foliaceus are not present; for you observe everywhere a smooth, apparently normal, skin, which only in some places presents vesicles or the scars left by them.

3. At times the patient also showed—there is little to be seen of it now—condyloma-like excrescences which suggested pemphigus vegetans.

If we take these three facts into consideration, I think I may be justified in assuming that we have here before us a remarkable combination of different signs, each of them bearing in itself the character of malignancy.

The patient is, on the whole, in a comparatively very good state of health; at any rate, remarkably better than on his admission in December of last year, which is in all probability due to the better surroundings in which the patient, who belongs to the least well-to-do class of the population, is now placed. Whether the affection in itself has been influenced by the medical treatment we employed is, of course, difficult to decide. The fact, however, that traumatic epidermolysis still continues, and the reappearance of vesicles on the skin —*even on the scalp*—as well as on the mucous membrane of the mouth, pharynx and larynx, are a little in favour of the presumption that the nature of the disease had been actually influenced.

On the other hand, in our patient, as in other cases of pemphigus, I have been fully impressed by the *excellent results following upon the administration of injections of strychnine*

which had been regularly used for some months. Though I recognise the beneficial effect of the local application of tar, yet, as regards the favourable course of the case in question, I am forced to consider it as essentially due to the general line of treatment. Experiments with Brown-Séquard's fluid had no effect whatever.

The injections are almost painless. One has only to guard against the setting-up of nervous irritations by the use of strychnine either by too large single doses or by a too long continued use of injections.

The treatment of the throat has mainly consisted of painting with 10 per cent. solution of arg. nitr., which we not only employed when the vesicles were developing, but also as a prophylactic.

I do not intend to go into any further details. Dr. Westberg, as stated, will somewhat later dwell largely upon that subject. I will only direct attention to two points. In all places which were frequently attacked by vesicular eruptions, and where the skin had consequently become atrophied, especially on the extensor parts of the arms and the region of the scapula, there is to be found a very large number of small white nodules, as large as a millet-seed at the most. If the wrinkled epidermis be torn off, which is very easily accomplished, these white nodules remain, partly on the under surface of the torn-off horny shreds, but partly on the reddish moist surface that now comes into view. Probably they represent those excrescences that are described by many authors as "milieux." Dr. Sasakava has examined these formations, and has ascertained the fact that they do not represent an affection of the sebaceous glands, and hence the term "milieux" is inadmissible. Moreover, they resemble *hollow cyst-like globules of epithelium*, which seem to me to have originated from the *duct of the sweat glands.* Possibly they may correspond to the "cystes épidermiques," which were described by Brocq and Hallopeau in some cases.

Again I regret that I cannot accept Dr. Kromayer's statement that in pemphigus a separation between epidermis and connective tissue takes place. Neither the microscopical examination of the excised parts confirmed his assertion, which *à priori* seemed to be very improbable, nor did we

succeed in obtaining the same results by imitation of his experiments, namely, by "allowing the contents of the vesicles to act upon skin-cuts."

In conclusion, I wish to recommend to your consideration the use of strychnine, either by administering it internally or in the form of injections.

A CONTRIBUTION TO THE STUDY

OF

DERMATOSES PRODUCED BY DRUGS.

BY

DR. JADASSOHN,

of Breslau.

TRANSLATED

BY

L. ELKIND, M.D.

A CONTRIBUTION TO THE STUDY OF DERMATOSES PRODUCED BY DRUGS.

By Dr. JADASSOHN.

The "drug-exanthemata" have—especially since the publication of Koebner's famous article—of late occupied a prominent place in literature. Their important bearing upon the study of the pathogenesis of some of the so-called idiopathic dermatoses has been repeatedly emphasised, and contributions dealing with that subject have been diligently collected. As regards our knowledge of it, perhaps no progress has been made. Its definition, its demarcation in reference to what belongs to it, and, finally, the classification of what is already known to us, encounter difficulties which are, one must admit, increased by the practice among German writers of describing it as "Artznei-Exantheme" (drug-exanthemata), for, generally speaking, we use the expression "exanthemata" to denote chiefly those dermatoses which, like the "acute exanthemata," are due to a cause which invades the whole system, and we do not relish this denotation when applied to a merely local irritation as well as to the isolated efflorescences, which, for example, follow the use of the salts of iodine and bromine. So it seems to me to be preferable to use the more general expressions employed in foreign literature, such as: "Drug eruptions," "Eruptions artificielles" (médicamenteuses). Under these heads comes everything which at all deserves to be mentioned here, and, indeed, it is necessary, as regards the present state of our knowledge, to avoid a separation, a view which is also advocated by Morrow in his well-known book.* Against the introduction of an artificial separation two reasons of the utmost importance may be advanced here.

* Drug Eruptions, New York, 1887, pp. 3, 4. Reprinted in New Sydenham Society's Library, Vol. 143.

First, the fact that the expression, "exanthemata produced by drugs," in its signification implies also that of "idiosyncrasy" to an almost inseparable degree. This custom of denoting, which we certainly cannot dispense with, plays here, rightly and naturally, a prominent part. For only those effects of drugs on the skin deserve in actual practice a careful attention which are unusual and unexpected, and hence reveal a peculiar idiosyncrasy. But theoretically the separation of exanthemata depending on idiosyncrasy is not admissible. Where is the distinction to be drawn between the reddening of the face after the use of amyl nitrite and the transitory "rash" without any visible inflammatory signs—such as can occur after every possible drug—and between the latter and the severest antipyrin-pemphigus? There is, as Brooke* rightly describes it, "a continuous and gradually-progressive series, extending from those which occur with almost absolute regularity ('specific') to those which vary in every individual." There are drugs which always produce dermatoses, some which often do so, and others again which very rarely have that effect. On the other hand there are drugs which, if taken in a large dose, produce skin affections in every case; in a small dose, only in certain individuals. The nature of these dermatoses does not depend upon the character of the drug; they all come under the heading of "drug-eruptions." This being the case, how is one to know where "idiosyncrasy" sets in?

Another and a somewhat more weighty point seems to me to be in favour of the maintenance of a definition as general as possible, and this brings me to my own subject. This is *the differentiation between the dermatoses which follow the external application of drugs and those which appear after their internal administration.*

This distinction was especially urged by Koebner† as absolutely necessary. "In no case," he says, "was he able to recognise a similarity or even to approve of the use of the same name," and this on account of the fact that "inflammations of the skin as produced by the application of drugs

* Monatshefte für prakt. Dermat., 1890, Bd. XI., p. 193.

† Verhandlungen des X. Internationalen Medicinischen Congresses, Berlin, 1892, Bd. IV., abthlg. XIII., p. 36.

in persons with a skin specially susceptible to inflammation are much more localised, develop gradually, and run a quite irregular course, and thus present a form of simple artificial erythema or eczema and so forth; what extension their further spreading assumes is in itself quite unimportant, however in some individuals they may even form small petechiæ." As points of differentiation he advances: "the tendency to observe strict continuity in their extension from the original seat, no matter at what point the drug has been applied, the non-involvement of the mucous membranes, and the fact that the sensorium remains unaffected."

This view, which did not entirely agree with that of Fox,* as Koebner thought, had to be controverted in different ways. The arguments against it are various. After the external application of drugs we have all seen how dermatoses may suddenly and regularly appear in an individual, and always run the same course. They do not always spread in a direct line, but "shift about," as Fox says; they appear —and this is the most important—not exclusively in persons with a particularly tender skin; in these also idiosyncrasy plays a most conspicuous part. Persons, who are certain to react to a drug which in general is not irritating, experience no injurious effects from other really irritating substances. We must, as Besnier† does in regard to "toxicodermias," make a distinction between eruptions produced by external application of drugs in patients who react to one, and in patients who react to several agents. In the former idiosyncrasy plays as necessary a part as in the "drug-exanthemata," after internal administration described by Koebner.

The reasons which L. Lewin‡ gives against the separation of the two classes need not be discussed here. They seem to me the less conclusive because his arguments exclusively apply to the drug; in my opinion it must be admitted that, even if the mode of action of drugs used internally and externally were totally different, the same remedy in different patients may at one time produce effects entirely opposite to

* Contribution to the Study of Drug Eruptions. The British Journal of Dermatology, 1890, Nov., p. 327.

† Annales de Dermatologie et de Syphiligraphie, 1895. Nr. 7, p. 649.

‡ Betrachtungen über Arznei-Ausschläge, II. Internationaler Dermatologischer Congress, Wien, 1893, p. 250.

those observed at other times, and that therefore the skin diseases from internal and external application of the same drug could easily be classified. The deductions resulting from Koebner's view are also found in Brocq's work,* who, in imitation of Bazin, divided artificially produced eruptions into those "à la suite de contacts irritants directs" and those "provenant de l'ingestion de certaines substances toxiques pour l'économie"—a division by which a number of substances are again brought back to these two groups.

According to this view the mode of use is the real means of distinction. But L. Lewin, in his valuable work which treats the subject almost exhaustively, endeavours to prove the contrary, and represents the mode of use as unimportant.

Surely in this conflict of opinions the less prejudiced view must be the right one, and therefore the division of drug eruptions into two classes ought at present to be abandoned. But even should it be thought desirable to come to a definite conclusion on the classification of drug eruptions, a thorough study of the significance of the methods of medication will be required, and may lead to the knowledge of their pathogenesis. The individuality of the patient is so important that only observations on one and the same person can be taken into account. The question to be considered, therefore, is the following:—

What effect have the different methods of application of a certain drug on persons who show a decided idiosyncrasy to it?

Very little in answer to this question, as far as I know, is to be found in literature. The fact that the various methods of application of Hg. produce exanthemata does not prove Rosenthal's view "that the mode in which mercury is introduced into the body has no effect upon the nature of the exanthemata."

Only four cases are mentioned by Beyer†; two (one of his own, the other Rosenberg's‡) were treated with salicylic acid,

* Traitement des maladies de la peau, 2nd Edit.

† Ueber mercurielle Exantheme. Berliner klinische Wochenschrift, 1895, Nr. 23.

‡ Ein Fall von Salicyl-Exanthem. Archiv. für Dermatologie und Syphilis, XXVIII., p. 131.

one (Comano's*) with morphine, one (Lesser's†) with Hg. Rosenthal‡ mentions, as treated with Hg., the cases given by Bürtzeff§ and Engelmann.‖

I may also mention the following cases:—The third case observed by Morel-Lavallée¶ ("Hydrargyrie de cause interne —Liq. v. Swieten, puis pilules de protoidure—et de cause externe—emplâtre de Vigo, puis frictions mercurielles"); one case mentioned by Dubreuilh** (after gray ointment had been rubbed in locally for a trichophytia and calomel taken by the mouth); a case of Robinson's†† (external and internal use of calomel); a case of Fournier's‡‡ (inunctions, sublimate baths, injection of hydrargyrum nitricum, mercurous iodide pills; a case of Watson's§§ (Hg. pills and sublimate used externally); one of Ascherson's (calomel internally, Hg. externally).

Finally, the references bearing upon this subject are far from complete. I should like to add an observation of Allen's,‖‖ who, in a patient presenting an acquired idiosyncrasy to quinine, was able to produce an eruption by the administration of the drug, either by the mouth or the rectum, by subcutaneous injections, by the application of ointments, or even by making the patient keep the drug for about 15 minutes in his mouth.

On the other hand, I would cite a case of Rammally's,¶¶ who, after two mercurial inunctions, observed a severe dermatosis, whilst an injection with sublimate oil produced no injurious effects; a case of Ehrmann's,*** in which the eruption made its appearance after inunctions and an injection of oleum cinereum, but not after internal administration of Hg.

* Deutsche medicinische Wochenschrift, 1888, Nr. 14.
† L.c.
‡ British Dermatological Journal. Dec., 1891.
§ Berliner klinische Wochenschrift, 1879, Nr. 43.
‖ Revue de Médecine, XI., June, 1891.
¶ Annales de la policlinique de Bordeaux, 1889, I.; Morel-Lavallée, Obs. V.
** Bull. thér., 8. IV., 1890; cf. Morel-Lavallée, Obs. VI.
†† Morel-Lavallée, Obs. VIII.
‡‡ ,, Obs. XI.
§§ ,, Obs. XII.
‖‖ Acquired Idiosyncrasy for Quinine, New York Medical Record, 1895, Nr. 4.
¶¶ Journal des maladies cutanées et Syphil., 1892. p. 128.
*** Wiener med. Wochenschrift, 1893, No. 33, 34.

A similar experience is recorded by Ledermann*—an exanthema resembling scarlatina after inunctions, injections and external use of calomel; by the mouth it had no effect. As far back as 1884 Alexander† has described a case in which calomel produced no ill effects, but the application of a precipitate ointment produced an affection of the skin.‡

From these few examples it is evident that the method of administration of Hg. is not indifferent; it does not appear "obvious" to me, as Rosenthal states, that "exanthemata after external use of mercury are infinitely more frequent than after any other form of medication." It would be more to the point to find a reason for the fact that exanthemata after internal administration of calomel—which is at least used as frequently as gray ointment—are so rare that Ferdinand Hebra could ignore their occurrence. I here report two cases lately come under my observation which will serve to illustrate the difference in question.

A female patient under my care, who was treated for pediculi pubis, with a pure§ gray ointment, and later with the application of a gray plaster on the arm, presented affections of the skin, the one arising in the inguinal and spreading up to the axillary region, not showing any tendency to become diffuse; the other affection, however, extending from the part where the plaster had been employed, took a diffuse course. Again, not even the slightest inflammation followed the application of repeated injections into the urethra and bladder, consisting of hydrargyrum oxycyanatum (1:500), of subcutaneous injections of thymol-mercury (0·1:1·0 paraffin. liqu.), and of the internal use of calomel (0·3).

On the other hand, I lately met with the following case. A robust young man consulted me last year for extensive dermatitis, the result of an inunction with gray ointment, which had been prescribed for pediculi pubis, and had caused

* Berliner Dermat. Vereinigung, Mai, 1892; Archiv. für Dermat. und Syph., XXIV., 1892, p. 905. Rosenthal also cites this case in support of his view of the unimportance of the mode of application.

† Archiv. für Dermatologie und Syphilis, 1884, p. 105. A. mentions that Biermer, who prescribed much calomel, never observed an eruption after its use.

‡ I could only find a short notice of a case of Petrini's, with "intolerance intus et extra" (Annales de Dermatologie et de Syphilographie, 1891, p. 223).

§ I mention this in reference to the importance attached by Neisser (v. infra) to the impurity of the ordinary grey ointment of commerce.

general disturbance of health. At the time I could not ascertain whether pure or impure gray ointment had been used. He came later to me with an ulcerating chancre, which, not remembering the past, I powdered with calomel. Next day the skin of the penis was red and swollen; the dermatitis extended over the inside of the thigh, but did not spread any further. After explaining to my patient the state of affairs, and telling him that in my opinion every effort must be made to accustom him to Hg., I applied a piece of gray plaster (5 cm.^{2}) on the upper part of the left arm. The following day the epidermis under the plaster was raised in a blister, the spot was surrounded by a redness resembling that of scarlatina, extending to the shoulder and the wrist, and also along each side of the thorax. There was very little fever, but serious subjective troubles. The eruption disappeared after a few days. The patient now took at night 0·03 hydrargyrum oxydulatum tannicum. During the night there was much burning of the skin and fever. Next morning he presented a characteristic picture; *from the neck to the knees the skin was intensely red, itching and burning, but the parts which had been powdered with calomel and covered with the gray plaster were exempted with almost mathematical precision*, so that, for example, on the left arm the redness only began at the wrist. The mucous membrane, as before, had remained unaffected. (As a peculiar feature, I may mention, without enlarging upon the fact, that during the last general eruption the thyroid gland was swollen in a very marked manner, and painful at the slightest touch.)

This patient, therefore, in contrast to the preceding case, had an idiosyncrasy *to both these methods of prescribing Hg.* The connection between the symptoms after external and internal administration of the drug is still more clearly demonstrated by the "local immunity," which showed itself after the dermatitis had been caused by external medication, and this is analogous to the acquired immunity which Samuel found in his well-known experiments with Croton oil.*

At a later stage I shall refer again to the general importance of these observations. I will now add a practical remark on idiosyncrasy to Hg.

* Virchow's Archiv., Bd. 127.

Fournier* discusses the question, whether in syphilitic patients with an idiosyncrasy to Hg., it would be advisable to make a change in the preparation or in the method of administration, but leaves it unsolved. From existing data I would observe that a change in the preparation seems to afford but little chance of success; irrespective of the fact that in sensitive patients the most different forms of preparation have produced eruptions, we have no absolute proof that the Hg. which enters the body even in the various *forms* of preparation—I do not speak of quantity—is absorbed. A change in the *method* of medication is, however, admissible, if not fully indicated, on the strength of the above experiences which point to the importance of the indication of the absorption of Hg.; for, judging from the evidence at hand, it does not seem doubtful that the absolute idiosynerasy, *i.e.*, an idiosynerasy which displays itself with every form of administration of Hg., is rarer than that with external use only. I would therefore prescribe for a patient, who shows dermatitis after the use of gray ointment or gray plaster, a cautious trial of internal medication or subcutaneous injections, which, in the case of the woman referred to above, proved successful.

As to the other question, namely, whether a person who exhibits exanthemata after taking Hg. by the mouth would feel no ill effects from it used externally, I cannot speak from personal experience; and I have found only one case, the interpretation of which, in this sense, seems doubtful, and to which I will refer later on.†

Two causes tend to render the explanation of all these cases still more difficult. In the first place, the specific reaction generally, but not invariably, takes place after each application of the drug in question; and, secondly, *habit* plays an important part. This can, as shown in the above case, be limited both as to time and *place*; it can be produced suddenly (after one large single dose, followed by severe dermatitis), but can also be acquired by small doses.‡

We do not know whether the experiment would be success-

* Traitement de la Syphilis, p. 145.

† Morel-Lavallée, l.c. Cf. also Annales, 1892, p. 851.

‡ Such is the case of Galowsky mentioned in the discussion.

ful in all cases, but the case we have cited* proves that there is a chance even with very sensitive subjects. The habit lasts for a longer or shorter time. If a really durable immunity is ever attained, I am unable to say; but cases are recorded which seem to prove that idiosyncrasies may definitely disappear in the same way as they have been acquired.†

Morel-Lavallée, therefore, quite correctly concludes his observations on this subject with the remark: "Ce sera affaire de tâtonnements."

After dermatitis from external application of Hg., that caused by iodoform has been during the last years the most frequent theme of discussion. Eruptions from this drug also require a special predisposition, a certain idiosyncrasy. Iodoform, which in itself has no irritating effect on the skin, causes in some individuals (who, from my own knowledge, feel no bad effects from other really irritating substances), even when given in the smallest dose, a dermatitis which either remains local or extends more or less over the body. The division proposed by Fox‡ into three groups according to the extent of the spreading, seems to me artificial, because a continuous gradation exists from the localised to the general form.

In the five cases which I have been able to investigate during the past years the eruption appeared after a minimum dose in each case in the form of erythematous or vesicular dermatitis, even in cases where the skin was uninjured, a fact to which Raynaud§ draws most particular attention. L. Lewin‡ seems to hold the opinion that when the skin is un-

* Remarks added during correction of proof. I accustomed my patient systematically to the use of Hg. At first he took 0·01 Hydr. oxydul. tann.: no sign of inflammation. I increased it gradually, without interruption, to 0·1 three times a day. At present the patient takes gray plaster and injections of 0·01 sublimate saline solution without ill effects.

† It is a well-known fact that also in iodism there are many possibilities. Some patients cannot get accustomed to IK even after prolonged use; others react only at the first administration. I lately noticed that a single dose of IK may produce immunity for a considerable length of time. A patient, after taking one grain, was troubled with œdema of the eyelids, coryza, headache, &c. Ten days later he could take rubidium of iodine without discomfort; a fortnight later, when IK was prescribed again, he took it without any ill effects. This proves how difficult it is to know the various actions of the different preparations of iodine even in the same patient.

‡ L.c.

§ Annales de dermatologie et de Syphiligr., 1895, p. 227.

injured only localised eruptions occur. (Is it because no absorption takes place?) But the experience of Raynaud is against this view; and on the other hand, in cases where the skin was uninjured, I have observed no further extension of the eruption, if proper precautions had been taken for the localisation of the iodoform. The possibility of a contrary result is, however, not to be denied.

As to the idiosynerasy of the organism, especially the skin, to the various methods of using iodoform, but few references are found in literature. Neisser* mentions that in two cases under his observation internal use of iodoform had no injurious consequences. Brocq† and Wolff,‡ in general terms, maintain that eruptions from iodoform also occur after internal administration. Morrow makes the same statement. Ducrey§ says that every preparation of iodine can cause exanthemata when idiosynerasy exists, and that the form of medication is immaterial when the drug is absorbed in sufficient quantity. Lewin also says that "both external and internal use of iodoform can produce secondary effects on the skin." He mentions as such acne and purpura, and does not mention the difference between this process and the ordinary dermatitis resulting from external use of iodoform. Still, purpura, as a result after powdering with iodoform has, as far as I am aware, only been once observed by Janowsky.‖ Eczema, after internal use of IK, is, notwithstanding the case mentioned by Caspary,¶ a very rare occurrence. Koebner explains the infrequent appearance of exanthemata after use of iodoform by its almost complete insolubility in the gastric juice, and the small amount of free iodine which is decomposed in the skin itself compared to the ease with which the salts of iodine and of bromine are brought into solution and division.**

* Ueber Iodoform Exantheme, Deutsche medicinische Wochenschrift, 1884, Nr. 30.

† L.c.

‡ Lehrbuch der Haut und Geschlechts-Krankheiten, 1893.

§ Revista internaz. di Med. e Chir., 1886; Ref. Archiv. für Dermat. und Syph., 1887, p. 625.

‖ Cf. Archiv. für Dermat. und Syph., 1884, p. 495.

¶ Archiv. für Dermatologie und Syph., XXVI., Bd., p. 11.

** Zeissl (Allg. Wiener med. Zeitschrift, 1881. Nr. 45) notwithstanding frequent internal use of iodoform, has never met with subsequent exanthemata.

The author, therefore, places the action of iodoform due to idiosynerasy in the same class as that of other preparations of iodine, more especially that of iodide of potash. We are only too ready to admit that if iodoform is absorbed and broken up in the body it may produce in predisposed persons acne, purpura, pemphigus, and, in very rare cases, also eczema. But the fact remains none the less that the most frequent effects produced on the skin by the salts of iodine are quite different from those usually manifested after the use of iodoform; and, in fact, Koebner ought to have pointed out this difference, because he has always insisted on the significance of the *quantitative action* of the salts of iodine and the appearance of acne after a rather prolonged use of the drug, in contrast to the sudden development of drug-exanthemata from true idiosyncrasy. This difference also exists with regard to dermatitis caused by iodoform, which almost invariably occurs after the first dose of the drug.* Other authors readily admit it; for example, Boekhardt,† who writes: "Skin eruptions, resembling those caused by ingestion of IK (iodine acne) often appear after internal use or subcutaneous injection of iodoform. A special form of exanthem, peculiar to iodoform, however, is produced in persons so predisposed, namely, those with an idiosyncrasy to this drug."

In order to prove that the idiosyncrasy to iodoform and that to other preparations of iodine are not identical, I have tried the drug in its various forms on patients in whom external use of iodoform caused eruptions. In no case did internal administration of IK produce iodism; on the other hand, I have been able to apply iodoform externally without bad results to persons who manifested a strong idiosynerasy to IK; external application of iodide of potassium, iodates, aristol, europhen, iodol, and lorentin caused no eruptions, even when these preparations were, for a comparatively long time, brought into contact with an injured or slightly injured skin; in some cases even painting with a tincture of iodine was prescribed without resulting in dermatitis. Against these experiences I have only found one reference—

* An exception to this rule is mentioned by Treves (Practitioner, 1886, p. 171).
† Monatshefte für practische Dermatologie, 1886, I., p. 10.

that of Raynaud,* who mentions that in the case of a female patient tincture of iodine produced *a very slight skin affection*, and a notice from Holsten,† who, in a predisposed person, had seen a slight dermatitis after the use of aristol.‡

Notwithstanding these authorities, I feel justified in concluding, from the above cases and clinical experience, that the peculiar property of iodoform, which causes acute dermatitis in predisposed persons, *must be attributed to the iodoform itself and not to the iodine it contains.* It cannot be considered as a quantitative action of the haloid salt, for, in the majority of cases, eruptions appear after the first dose. Subsequent experiments have convinced me that they must not be attributed to the CH_3 group present in iodoform, for they did not make their appearance when some of the patients were painted with chloroform and bromoform, which are similarly composed. It may therefore be said that the power of iodoform to produce dermatitis, when a predisposition exists, is as inherent a quality of this drug as its toxic and antiseptic properties, which cannot be ascribed to the simple action of the iodine.

All my patients reacted only to the external application of iodoform. In agreement with the two cases mentioned by Neisser, I also failed to produce the slightest effect on the skin by internal medication (iodoform in capsules or pills) continued for several days; general disturbance also remained absent. The same negative result followed on repeated *subcutaneous* injections of iodoform oil (1 cem. of a suspension of 5 iodoform in 30 of olive oil, of which only a small quantity is dissolved) when the skin had been previously rendered impervious to the action of iodoform by being thoroughly bathed with pure oil before and after the injection.§

A still more remarkable experience I have had with two similar patients, *whose wounds could be powdered with iodo-*

* L.c.

† Medical News, LXII., Nr. 2.

‡ Israel (Therap. Monatsh., 1889, p. 95) mentions that in a case of iodoform idiosyncrasy the use of iodol had no irritating effect.

§ Once I succeeded in introducing into the skin a small drop of this suspension; but similar experiments are very difficult, it being almost impossible to screen the surface entirely from contact with the iodoform.

form without producing dermatitis, by preventing the iodoform from coming into contact with the edges of the wound, which can scarcely ever be avoided in ordinary practice.

In a patient with a large ulcer, following removal of buboes, the iodoform could be dusted on the centre without producing any ill effects, while an external application of the same agent on any other part of the body, though the skin was intact, produced inflammation, and even the application of iodoform on the bubo showed clearly the idiosynerasy of the patient to that drug.

The same had been observed in the case of an elderly woman, the subject of an ulcer of the leg, and also in a patient who was known to react on the application of iodoform, whilst the dusting of the latter on a raw surface, produced by the use of a blister of eantharides, remained without any ill effects.

These experiences having led me to conclude that, even in the ease of strong idiosyncrasy to iodoform, an immediate contact of the drug with the skin is necessary to produce the reaction, I resolved to test, on three of my patients, the susceptibility of the *mucous membrane* to iodoform. The drug was introduced, partly in powders, partly in oily suspension, into the mouth, nose, rectum, and urethra, care being taken not to touch the skin. Not the least sign of inflammation, either subjective or objective, was observed, although some parts, especially the nose and the rectum, had been exposed to the action of the iodoform for a sufficiently long time.* On the other hand, the powder put into the external auditory canal produced a decided eruption with injection of the membrana tympani—a clear proof that this covering is really of the same nature as the skin.†

It is, of course, in no way my intention to generalise; to maintain that in all persons with an idiosynerasy of the skin to iodoform the mucous membranes are at all times "immune" against the action of iodoform. But the contrary assertion, that the mucous membranes are particularly sensitive to the

* Geyer (Ref. Therap. Monatshefte, 1889) thinks that "at least" contact for half a minute of the iodoform with the skin is necessary.

† G. Legiehn (Therap. Monatshefte, 1892, Nr. 4), who after insufflation of iodoform into the external auditory canal twice witnessed a dermatitis.

action of iodoform, is equally unwarranted. For, if in a few instances mentioned in literature, *e.g.*, by Raynaud* and by Herzfeld† (vagina, urethra), the use of the drug has caused a dermatitis, the possibility of a contact with the skin may have been overlooked in these cases.

On the strength of my observations, I must, therefore, at present, consider as improbable the view expressed by L. Lewin, that, in cases where the drug has not been brought into contact with the skin, the dermatitis proceeds from its primary action on the accessible mucous membrane. Nor do I agree with the view that the by-effects of iodoform after internal medication are so seldom witnessed because the drug is so seldom prescribed. My observations on five successive patients seem rather to prove that usually the idiosyncrasy to iodoform manifests itself only after external application.

My experience also contradicts the following statement of Koebner's, that "the very rare appearance of exanthemata after internal administration may be explained by the complete insolubility of iodoform in the gastric juices, and the very small quantity of free iodine which is decomposed in the skin." For, in subcutaneous injections, there is no question of its insolubility in the gastric juices. Moreover, we have obtained proofs that, both after injections and the use of iodoform capsules, the iodine reaction could be shown in the saliva an hour later.‡

In now proceeding to draw conclusions from the results obtained by my investigations, I am fully aware that the greatest caution will be necessary; for a single experience in the other direction, in a field where surprises are so manifold, may overthrow the most beautifully-devised hypothesis.

* Annales de Dermatologie et de Syphiligraphie, 1895, N. 3, p. 227.

† New York Med. Record, 1893. N. 8, p. 233.

On the other hand Cathelineau distinctly mentions the exemption of the mucous membrane in a severe case of iodoform dermatitis of the penis.

A case of Bolowski's (La Pratique Médicale, 29, XI., 1887) is unfortunately not accessible to me in the original, but a reference states that the introduction of an iodoform suppository into the uterus caused toxic symptoms and skin eruption.

‡ Rummo (Arch. de physiol. norm. et pathol., 1883, p. 307) obtained the same results in his experiments on dogs. He mentions that when iodoform was introduced per os or injected into the peritoneum, the iodine reaction could be shown in the saliva from 1 to 1½ hour later, and by injecting an ether solution under the skin after only 10 to 20 minutes.

I will therefore restrict myself to the exposition of the various explanations to which the question lends itself.

The fact that in three cases the mucous membrane proved immune against the immediate contact of iodoform, and in one case against mercury, whilst the skin reacted, seems to me an additional indication of a fact, which is not always sufficiently kept in view, that mucous membrane in contiguity with the outer skin really differs from it in every respect—physiologically as well as anatomically. To whatever cause we ascribe the "specific susceptibility" of the skin to irritation, it differs from that exhibited by the mucous membrane. In confirmation of this statement I may mention the result of an experiment which I lately made. Stinging-nettles, which, on the slightest contact with the skin caused severe urticaria, could be kept in the mouth by myself and several colleagues without other effect than a brief burning sensation, and without producing either redness or swelling. Factitious urticaria of the mucous membrane is also unknown. When the mucous membrane is affected by the administration of drugs (as in the case of acute exanthemata), the eruptions bear no comparison with those produced on the skin by irritating substances from without.

Again, the idiosyncrasies are not exhibited by the whole body, but appear only in single organs or system of organs. A person, who, after the use of salicylic acid is invariably troubled with erythema, may remain free from tinnitus aurium, whilst in the majority of people the opposite takes place. Minimum doses of Hg. may in one patient cause stomatitis or enteritis, whose skin remains unaffected even after use of large doses, and *vice versa*. These differences in the susceptibility of single organs has been specially pointed out by Lesser. They also exist between the skin and the mucous membrane. In fact, I shall be able to prove later that in this respect the skin ought not to be considered as an organ of which all parts show a uniform reaction, for it exhibits also "localised idiosyncrasies."

Besides, the fact that iodoform could be introduced harmlessly into a wound, whilst at the same time the skin was known to react to the drug with unerring certainty, proves

that a special susceptibility of the skin, or, as in the case of the plaster of cantharides, of its outer layers, was present in my patients; unless—and to this I will refer again—the decomposition of the iodoform through contact with the fluids of the body prevented the dermatitis.

Returning to the question mentioned before, respecting the different manifestations of dermatosis after internal and external medication, the results obtained should warn us against drawing general conclusions from a few single observations. On the one hand we have the evidence, especially with regard to Hg., that an idiosyncrasy may exist in the same individual to both its external and its internal use; also, that, with idiosyncrasy to external use, the drug may be tolerated per os or by subcutaneous injections. On the other hand, my experience with iodoform has proved that in cases where a decided predisposition to effects from its external use exists, every other form of medication may fail to produce reaction. It is quite obvious that the strict differentiation of the effects of the external and the internal action of Hg., for which Koebner gives general laws, cannot be maintained. Not only do the clinically identical symptoms prove this—irrespective of the general dissemination of Hg. dermatoses after internal medication—but also the cases, to which Lesser has first drawn attention, where idiosyncrasy to both methods of medication is apparent, and especially the case described by me above (in which the localised dermatitis induced from without caused local immunity to internal administration) makes the identity of the pathogenesis in both processes very probable.* On the other hand, there are well-authenticated cases in which only the external application of Hg. called forth the dermatitis. The eruption may extend over the whole body, it may also be limited to the area of medication and its vicinity. Even if it disseminates, it does not spread so regularly as the dermatitis after internal use, but it settles in certain spots, as the armpits, the elbows, the neck—it "shifts about."

* In reference to this point it must be remarked that the immunizing action of the eruptions caused by use of croton oil, discovered by Samuel, is really a specific action, viz., one which exclusively or preferably protects against inflammations caused by the same agent.

Here I must meet another objection that may be raised. It is a well-known fact that even persons with an excessive idiosyncrasy to Hg. may get accustomed to its use even after a single trial. It may be argued that the absence of deleterious results from internal medication after external had produced dermatitis was due to the body having become accustomed to the drug.

This objection seems to be unwarranted, first, because the great difference in the frequency with which dermatitis appears after internal and external use of drugs points to a difference in the conditions necessary for their relative occurrence; secondly, as in the first-mentioned case, after a circumscribed skin eruption from gray ointment, internal administration and subcutaneous injections failed to produce the least sign of it in any other part of the skin. Another answer to the objection may be found in a case mentioned by Fournier (l.c.). In a patient, who for weeks had been able to take protoioduret without discomfort, one single inunction with gray ointment (for pediculi) at once caused dermatitis.

The next explanation of the difference between the action of Hg. by external and that by internal medication is that which takes account of the quantity, or rather the concentration, of the Hg., which is brought into contact with the skin. It is obviously much greater in external than in the most powerful internal medication. It might therefore be said that, where excessive idiosyncrasy exists, every particle of Hg. which touches the skin produces dermatitis, consequently also that which is taken by the mouth; but that, where but a slight idiosyncrasy is present, only larger quantities like those that come in contact with the skin in external medication induce the eruption.

The view that the quantity of Hg. to a certain extent is accountable for the appearance of dermatitis after internal medication, was also held by Morel-Lavallée*; and Ehrmann† has expressed the opinion that the rare appearance of exanthemata after internal use of Hg. must be ascribed to

* Revue de méd., 1891, June.

† Ergebnisse der speciellen pathologischen Anatomie von Lubarsch und Ostertag, 1896.

the fact stated by Ludwig, that the Hg. is absorbed from the intestine, is carried through the portal system into the liver, and from there with the gall back again into the intestine, and that therefore only a very small quantity enters the general system, and especially the skin.

Whether this view can be maintained with regard to subcutaneous injections is doubtful; for, even if by this method the Hg. were separated in the intestine and kept out of the circulation in the way described by Ludwig, it must be supposed that at the time the Hg. is circulating in the intestines it is present in the skin also. Ehrmann (l.c.), at least, has had a case under observation in which injection and inunction produced eruptions—but not internal medication. However, in this instance also the difficulty meets us that we cannot exactly determine what influence habit may have exercised over the further course of the eruptions; whilst, strange to say, under the first treatment the "erythema toxicum bullosum" only made its appearance after thirty-five inunctions, on a subsequent occasion an injection of ol. cinер. again caused an erythema, but one of hydrargyr. oxydul. tannicum, none. Later, however, as Ehrmann kindly informed me, a general, severe erythema followed an inunction, and a slighter inflammation a pill of protoioduret (0·01).

Even taking no account of the remarkable fact already confirmed from observations on the action of Hg. and other remedies, that at first a certain cumulative action was necessary to bring out, so to speak, the idiosynerasy,* which afterwards manifested itself at the first dose, the possibility still remains in the first case mentioned by Ehrmann that the inunctions and the subsequent erythema had not been sufficient to make the body immune, so that an injection of oleum cinereum could still cause an eruption, whilst inunctions and an injection had caused immunity against the internal use of Hg.; in the second instance, one inunction, and

* A similar case is mentioned by Morel-Lavallée, l.c., 1 Obs. (The appearance of an eruption after several weeks' treatment with protoioduret, twice every three days.) Cf. on the use of quinine, Landgraf, Verein für interne Med., Berlin. 1893; Koch, Deutsche Méd. Wochenschr., 1894, No. 38. Morrow, l.c., p. 8: It has been observed that one attack of a drug eruption seems to confirm and intensify the susceptibility to subsequent attacks.

more especially the erythema it produced, was insufficient to deaden the reaction. These conclusions are supported by the evidence that the reaction became each time weaker, as well as by cases quoted in medical works, in which one injection produced a severe erythema, a second a slighter one, and a third none at all.

Against the deduction of Ehrmann—however great its value may be—it must be remarked that medical records and my own observations prove that eruptions after injections are really much more infrequent than after external use of Hg.; and in this respect also the case just stated is valuable while it shows that an inunction could be tolerated without the least reaction, notwithstanding that a localised dermatitis produced by inunction had preceded it.

However, whether we accept or reject the interpretation of Ehrmann, the possibility remains that quantity is the most important factor in the different effects of the various modes of use of Hg. For, in subcutaneous injections also, the concentration of the Hg. which, through the circuitous route of the circulation, comes in contact with the skin, is much smaller than that which reaches it when applied externally. Single instances, such as, for example, the case lately published by Allegeyer and Sprecher,* where the erythema only made its appearance after injections of highly concentrated sublimate, prove that the concentration of the Hg. which comes in contact with the skin may have some influence on the result.

From these considerations we might come to the conclusion that the majority of people who possess an idiosyncrasy to Hg. only react to the strong, concentrated form generally prescribed for external use, and that but few people are so highly susceptible that they react also to the normal quantity which reaches the skin after subcutaneous injections or internal medication.

But, then, it would have to be supposed that there are people who can only tolerate internal and subcutaneous medication of Hg., but not others in whom the opposite occurs, who bear Hg. applied to the skin without discomfort whilst internal medication causes an erythema. I have

* Deutsche Medicinische Wochenschrift, 1895. Nr. 38.

already pointed out that only a single instance which seemed to prove this, reported by Morel-Lavallée, has come under my notice.

In this case an erythema, which was confined to the feet, appeared after protiodide pills had been taken for several weeks. When this had subsided emplâtre de Vigo applied to the chin caused no eruption; but as later on protiodide pills taken for a week caused no affection of the skin while finally six inunctions prescribed some time after produced a vesicular erythema, this case cannot be accepted as evidence. The only conclusive evidence would be a case where Hg. had been tolerated for a considerable time externally, and then suddenly, on the first attempt at internal medication, an erythema occurred; or one where several doses of Hg. given in regular succession by the mouth acted positively, and a number of external applications negatively.

Such evidence would overthrow the entire "quantitative hypothesis." In general this is not supported by our observations on the exanthemata from internal use of drugs. They rather tend to prove that the amount is of very little consequence—except in the case of acne from iodine and bromine.* Other hypotheses, therefore, should be advanced, which really take into account the chemical relations. It *might* then be supposed that most people have an idiosynerasy to the various preparations of Hg. before its combination with the albuminates, so that when it is brought into the system by internal or subcutaneous administration there is no reaction because it so quickly unites with the albuminates; but that, on the other hand, in some persons the Hg.-albuminates cause inflammation.

As far as we know, all the various preparations of Hg., provided they are soluble, act as the result of idiosyncrasy in the same manner. It is different with iodoform, with which the action of iodine is not always identical. The fact that in a great number of cases the iodoform only caused eruptions when externally applied may be explained in the same way as in the case of Hg.—that the dose of iodoform which in

* Cf. Morrow, l.c., p. 6. In a majority of cases, the quantity of the drug injected is immaterial, its irritative effects upon the skin being determined rather by the idiosyncrasy or susceptibility of the individual.

internal and subcutaneous medication comes in contact with the skin is too small. But the explanation seems ready at hand, that, as iodoform is internal and subcutaneous administration is decomposed, an action of undecomposed iodoform cannot manifest itself on the skin. On this hypothesis a dermatitis as effect of internal administration of iodoform is impossible. Consequently, the negative result from dusting the drug on the surface of wounds can be explained thus: the iodoform, decomposed by the secretions of the wound, does not *per se* come in contact with the skin. Therefore, where an idiosyncrasy for iodoform* exists there is a real difference between its action from within and that from without.

We do not know whether there are generalised dermatitides which depend on the absorption of iodoform from within or without. When Fournier,† in a remark made during a discussion, speaks of "rashs iodoformiques," and explains that they originate from within "like veritable cases of poisoning." it would be wrong to deny its *à priori* possibility, but the existence of such is far from proved, as it has not been made evident that the extension of the eruption through dissemination of the drug or the simple spreading of the inflammation from contiguity have been excluded. The absorption of iodoform from external application is not greater than from internal use or subcutaneous injections, therefore it will be necessary, in every case where investigations are made on the question of absorption, to be sure: first, that the dissemination of iodoform from outside was impossible; and second, that the action was due to the iodoform itself and not to the iodine it contains, as it is well known that IK also may cause erythemata and eczema.‡

* An opposite opinion is held by Crocker, who, although generally admitting the difference between exanthemata from internal use and eruptions from external medication, remarks with respect to iodoform that "as soon as it enters the body" it may cause erythematous or other eruptions (International Medic. Congress, Berlin, 1890). I do not know whether Crocker bases his opinion on special observations, mine at any rate contradict this view.

† Annales, p. 192.

‡ I cannot admit in regard to this fact the explanations which Harnack (Berl. Klin. Wochenschrift, 1883, Nr. 47) and Gründler (Diss. Halle, 1883) have given of the cause of iodoform poisoning. He maintains that the latter only occurs when the iodine at the spot where it is applied enters into organic combination and is absorbed. But Cathelineau brings forward a case to prove that in iodo-

These considerations amply prove that in every case of idiosyncrasy, and for each drug, the various methods of medication should be tested in order to discover the difference between internal and external administration. Besides the quantitative action on the skin, the chemical decomposition must also be taken into account, which, in one case, may call forth the dermatitis only after external application, in others only after internal use; for it is not difficult to conjecture —with Behrend—that through the assimilation of certain drugs, either in the alimentary canal or in the circulation, substances are produced which have an irritating action; but evidence of this is wanting.

Neither should the question of the locality *where* the irritating substances manifest their activity be answered by general statements. It scarcely admits of doubt that in the local action of Hg., as well as in that of iodoform, the inflammation is peripheral, whether we hold that its action is on the elements of the tissues, the coats of the vessels, or the nervous system; also with respect to the exanthemata after internal use or subcutaneous injections of Hg.—especially judging from the case of "localised immunity," referred to above—the most simple explanation seems to me to ascribe these to an immediate action of Hg. on the elements of the skin, which has reached it through the circulation and not to its action on vasomotor centres.*

The generalised skin affections appearing after external use can be explained in the same way, an explanation which is strengthened by the fact that the eruptions are most

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form dermatitis a difference, noted by Harnack and Gründler, exists between the indication of iodine in the urine before and after it has been reduced to ashes. Irrespective of the untrustworthiness of similar single observations and the difficulty of their application, it must be allowed that the symptoms of true iodoform poisoning are quite different from those of iodoform dermatitis, even when accompanied by high fever, &c.

* This view seems to be in accordance with Lewin's, who says (Die Nebenwirkungen der Arzneimittel, p. 36): "The natural explanation of drug exanthemata is, that the substances which enter the body, or rather the products of their combination or decomposition, either directly—or which is more rare, in a reflex way—produce exanthemata by means of the vasomotor or trophic nerves. Confirmation of this hypothesis would be found in cases where the noxious drug could be traced in the skin eruptions, and also in those in which the drug, such as for example salicylic acid, externally applied in the form of ointment, caused the same alterations as those produced by internal administration."

severe at the spots where the drugs are applied. But when they spread by "shifting about" it must either be supposed that the drug had been applied at the spots in question, or that at some places, such as the joints, it penetrates the skin most easily—through friction, tenderness of the skin, heat, &c., even when not immediately applied, or that (an external dissemination having been excluded with absolute certainty) these spots are particularly sensitive even to the smallest particle of absorbed Hg.* A uniform metastatic dissemination, in the sense in which Rosenthall accepts it, seems to me less probable, the substances in question being held in solution.

In other drugs than those discussed in this paper a central action may very possibly be the cause of the skin affections.

Only thoroughly exhaustive investigations of the different forms of medication can lead to the knowledge of the pathogenesis of the drug eruptions. As these are difficult, and as each investigator is able to make them on a small scale, I have thought it my duty to communicate the few observations which I could collect. They will, at least, serve to add a small quota to the facts already known in this field of investigation.

* This view seems supported by the fact that these spots (régions péringuinales et préaxillaires) are especially singled out also in internal "hydrargyrie" in its lighter forms (cf. Morel-Lavallée, l.c., p. 488). A case which I lately observed seems to confirm this statement. A patient who treated himself for syphilis by applying ointment to the extremities, noticed after a few days a diffused dermatitis on the scrotum and armpits. He assured me that the ointment had not touched these spots, and certainly had not been rubbed in. This dermatitis was followed by a slight folliculitis at the extremities. This case seems to me to point to a difference between folliculitis caused by inunctions and Hg. dermatitis. It is a well-known fact that certain spots of the skin show a special susceptibility to the action of substances taken by the mouth. Various observations prove this, especially the interesting fact recorded by Benzler (Deutsche Militärärztliche Zeitsschrift, 1894, Nr. 6), who repeatedly noticed a deep red spot at the right side of the back of the hand after use of antipyrin. A similar experience is reported by Ballin (Lyon méd., 17 Nov., 1895), who foun always the same spot affected in exanthemata from antipyrin.

MELANOSIS

AND

KERATOSIS ARSENICALIS.

BY

LUDW. NIELSEN, M.D.,

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TRANSLATED

BY

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MELANOSIS*

AND

KERATOSIS ARSENICALIS.

By LUDW. NIELSEN, M.D.

Although the belief in the curative effects of arsenic with regard to a very great number of diseases and to deranged states of health, notably in the case of affections of the skin, is no longer quite so unshaken as it used to be, yet the use and misuse made of this drug for therapeutical purposes is such an extensive one that its injurious by-effects ought to be noted with particular care, especially those not yet commonly known, namely, melanosis, and notably keratosis, which have been observed in the case of the patient whose history is given below.

R. J., aged 66 years, private individual, came under my care on the 18th December, 1894, for a slight recurrent balano-posthitis and cutaneous pruritus, which he had been suffering from for the last few months. There was also, as found on examination, a general pigmentation of the skin and keratosis of the palms and soles. These two affections had appeared almost simultaneously after a prolonged use of arsenic. Its application had consequently been suspended and the patient treated with an ointment consisting of menthol and salicyl. The following history was taken on the 8th April, 1896, when I again had an opportunity of examining the patient.

In his first youth he is said to have suffered from ague at long intervals for a few years, and some thirty years back he had an attack of gravel, otherwise had always enjoyed

* It is to be understood that the word Melanosis is here used by the Author in its general or etymological meaning, as applicable to deepening of colour approaching to black (see New Sydenham Society's Lexicon). English pathologists in former days applied the term to a black sarcomatous growth, but no such relation is intended by the Author.

good health, with the exception of a slight temporary outbreak of eczema about eight years ago. This relapsed at the beginning of 1893, and has remained since localised on the dorsum of the hands, on the wrists and the legs. He was put on Lq. arsenic. kalici. At first, for a short period, he was given 3 drops three times a day; later on regularly 5 drops three times a day, which was continued uninterruptedly for about a year (until 18th December, 1894), with the sanction of his medical attendant, who said that he could continue it for so long without any injury.

He is fair, strongly built, rather thin than stout, and not senile beyond his years. With the exception of the pathological changes of the skin, his health is perfect. None of the functions are in any way disturbed. The objective examination of the internal organs reveals nothing abnormal; urine acid, no albumen or sugar (the same had been registered on 18th December, 1894). During his use of arsenic no other signs of arsenical poisoning (on the part of the digestive organs, or the nervous system, &c.) are said to have set in except the present affections of the skin. After he had been taking arsenic for some months (his recollection of dates is not very exact), there gradually developed a brownish discolouration of the skin without antecedent erythema or itching; the latter, however, appeared somewhat later. His skin had always been "white and free from spots." Since the discontinuation of arsenic (some fifteen months ago) the colour of his skin has remained unchanged. The skin of the whole body, with the exception of the hands, shows a diffused brownish pigmentation, shading from a light café-au-lait tint to a dark coffee-brown. The skin of the neck shows the greatest pigmentation; in the region of the shoulders and on the upper part of the thorax it is less. The pigmentation is markedly less pronounced at about the middle of the body; from here downwards it again gradually becomes darker, so that the nates, the reg. inguin., the genitals, and notably the greater part of the thighs, especially above, on the front and the inside, are as darkly coloured as the neck. The pigmentation fades away again at about the crural region, where—just as on the arms—it is rather slightly developed, though a little more pronounced in the

bends of the joints. The skin of the face is the seat of slightly reddish spots, and also only faintly pigmented, so that his appearance is not much altered. Throughout the pigmented regions there are scattered numerous spots, situated very close together, and about the size of a pin's head, of decidedly lighter, whitish (query: normal) colour; these are especially marked on the most darkly pigmented parts. The other structures of the skin are not otherwise strikingly affected—the same applies to the condition of the hair and the nails. The perspiration is normal. At present there is no itching; it disappeared about a month after the suspension of arsenic. No other paraesthesis. No swelling of the glands. The mucous membranes are not attacked. Of the eczema referred to above there remained only a small plaque on the ulnar side of the right hand.

The skin of the volæ and plantæ gradually became diffusely thickened after the patient had been taking arsenic for several (query: eight) months; and it may be added that, neither before nor afterwards, had the occurrence of erythema, increased perspiration, nor any other subjective signs been noticed. Later on there appeared, simultaneously and gradually, small horny excrescences, even some time after he discontinued the use of arsenic. He had never done any hard work with his hands. The skin on the volæ—to a less degree, however, in the middle and on the radial side, especially of the right vola—and on the volar part of all the fingers, and to a certain extent on their parietal parts, is thickened, dry, hard, and of a dusky greyish appearance, especially in the sulci between the lines of papillæ. In addition, the affected skin is the seat of numerous scattered hard, horny excrescences of a yellowish-brown colour, ranging in size from less than a pin's head to almost as large as a pea; any particular localisation of these on the ducts of the sudorific glands cannot be distinguished with a lens. These horny excrescences must be cut away frequently (like corns) since they continually reappear. The skin on both plantæ —except in their hollow parts—and on the plantar parts of the toes is the seat of a diffused thickening similar to that on the volæ; there are, besides, the same kind of horny excrescences, somewhat more numerous and rather larger,

particularly on the left planta, and at the same time more flattened and pressed into the skin through walking. One especially, however, on the anterior plantar part of the left heel, is larger than the rest, and exactly resembles a small cutaneous horn, somewhat compressed, cone-shaped, slightly crooked, truncated, and provided with regular longitudinal striæ. Its implantation surface is from 3 to 4 mm. broad, and its growth presents an oblique direction, the smaller (about 4 mm. high) slightly concave surface of which lies in a small, nest-like depression of the skin, and may be slightly raised up. The height of its longest convex surface is about 7 mm. The horny excrescences of the plantæ soon reappear after their frequent removal in order to prevent inconvenience in walking.

After the use of soap and soda baths, and the application of salicyl plaster, separation of the horny excrescences ensued in about three weeks (the cutaneous horn had to be cut away). Their original seat, however, remained marked by small, roundish, horn-like indurations of the skin. The extensively-formed keratosis became softer. Later I lost sight of the patient.

Although arsenical melanosis has been known for several decades, it is only within the last few years, as shown from occasional reports, that it has attained greater attention. Indeed, in the large text-book of Kaposi* one looks in vain for a true primary arsenical melanosis. The most frequent form of arsenical pigmentation, which was also the earliest, and is the best known, are the brownish spots which often appear after the treatment of several skin diseases, and especially after psoriasis. They are not primary pigmented spots, but only a pigmentation of the skin where the disease had previously been located. Primary arsenical melanosis, such as is here considered, which usually appears in diffused patches, unconnected with preexisting dermatosis, is much more uncommon. This form of arsenical pigmentation may occur as a single symptom,† but usually it is associated with other symptoms; for example, digestive troubles, conjuncti-

* 1891. Annotated by Besnier and Doyon.

† Haffter, Wehlau, quoted by Holsti, and others. A bibliography will be found at the end of the pamphlet.

vitis, localised or general nervous affections of different kinds and various degrees, and, in a great number of cases, as in that of our patient, the melanosis is combined with keratosis vol. et plant., and in a few instances with other arsenical dermatoses, erythemata, zoster, and other vesicular and pustular affections.

This form of melanosis has been observed after accidental, acute and chronic poisoning with arsenic, as well as in cases where the drug had been medicinally used. Moreira reports some cases in which, a few weeks after acute poisoning with a rat poison containing a large amount of arsenic, a diffused brownish pigmentation of the skin occurred, with several other more or less acute symptoms in connection with the digestive organs, the nervous system, and the skin. In Barthélemy's description of 405 cases of arsenical poisoning at Hyères,* which resulted from the mistake of a wine merchant, who poured a solution of arsenic into the wine casks, he mentions—among other symptoms—in the greatest number of cases a pigmentation of the skin varying from brown to black. Similarly Kirchgässer often noticed, in cases of arsenical poisoning resulting from living in rooms with green-painted walls containing arsenic, distinct brownish spots on the face, and sometimes on other parts of the body. Gowers describes a patient who had for many years been engaged in painting with colours containing arsenic, and who developed arsenical tabes. As the cause of his disease was not recognised, he was treated with arsenic; a characteristic arsenical pigmentation at last led to a correct diagnosis.

Much has already been written on the appearance of pigmentation during medical treatment with arsenic in its various preparations, and the many internal and external complaints for which it is prescribed. Sex and age seem unimportant factors; in this, as in many other drug dermatoses, it is principally an individual predisposition, the origin of which is entirely unknown, which leads to its appearance

* Barthélemy draws attention to the complete analogy between these symptoms and the acrodynia which in 1828 and again in 1829 made such havoc on the western bank of the Seine at Paris, and caused the death of 40,000 persons in the course of from five to six months. He thinks that this mortality must also be attributed to arsenical poisoning.

after a most variable length of time, during which the drug has been administered. Usually, as in the case of our patient, the pigmentation occurs after the use of the drug for several months in the usual increasing doses; but in some cases it made its appearance after a few weeks' treatment,* and in exceptional cases only after several years. An example of this is the case mentioned by Mathieu: a male patient, aged 51 years, had taken daily, for 20 years, 3 to 4 eg. of arseniate of sodium "in order to keep up his strength." An attempt to increase the doses after nine years' constant use brought on gastro-enteritis, diffused bronze-coloured pigmentation of the skin, keratosis vol. and plant., and tabetic symptoms. Similarly in a case mentioned by Haffter, it seems that the pigmentation only occurred after several years' use of the drug. In a few cases the total amount of arsenic taken is mentioned; for instance, in a patient aged 23 years, with psoriasis, 30 eg. arsenic acid was taken in 3 to 4 weeks;† in a boy, aged 10 years, with Mr. Basedowi, 30 g. Lq. potash arseniate, in a couple of months;‡ in a boy, aged 8 years, with various nervous symptoms, 35 g. Lq. potash arseniate in three months;§ and in a girl, aged 19 years, suffering from anæmia and swelling of the glands, a general pigmentation like that of a mulatto appeared after an injection of 42 drops of Liq. Fowleri, and the internal use of 500 drops of the same remedy.‖

As arsenic not infrequently produces skin erythemata, it is not extraordinary that similar eruptions sometimes precede the pigmentation. The following are examples: acute general erythema after a few days from acute poisoning;¶ a form of erythema resembling rubeola and scarlatina.** Sometimes the two are simultaneous.†† Gowers, who minutely describes the initial stage of arsenical melanosis as consisting of small round patches of pigment, mentions the simul-

* Mueller, Schlesinger, Owen, and others.

† Mueller.

‡ Foerster, 1890.

§ Foerster, 1892. The pigmentation began, however, three weeks before the end of this period.

‖ Richardière.

¶ Moreira.

** Moreira, Cheadle (quoted by Schlesinger).

†† Morrow, Barthélemy, Ols. II., Holsti, and others.

taneous presence of corresponding erythematous spots, and concludes from this fact that the pigmentation is preceded by a congestion. But, judging from the observations reported on this subject, this does not seem the rule, and in general it appears that the melanosis may develop in various ways. According to Gowers, these small, round, pigmented spots enlarge and coalesce, leaving between them, however, some small rounded patches of skin which is unpigmented, or possibly on account of the contrast, appears whiter than normal. In other cases the pigmentation has commenced in more or less sharply-defined patches the size of a coin,* and it may also, from the very beginning, involve comparatively large parts of the skin. Moreover, in most cases, as in our patient's, we have to rely upon the patient's history with regard to the fully-developed condition of the pigmentation, and then it either presented itself as isolated patches, varying in size and number, or as a more or less general discolouration of the skin; the latter may also, at the same time, appear in smaller patches and large diffused spots. The very minute whitish patches, mentioned by Gowers, and a few other writers,† present a characteristic appearance; they were in our patient dotted closely and at irregular intervals over the diffused brownish pigmentation.

The colour is sometimes spoken of as dirty-grey. As a rule, it is brown in its various shades—bronze, copper colour, &c.—and may even, at least partly, be quite black.‡ Besides the pigmentation, especially in a more advanced stage, generally shows itself in different shades in the different regions of the skin, and most frequently attacks those parts which were involved in our case, namely, the neck, the back, and the upper part of the thorax, which were very dark; the middle of the trunk, however, remained much lighter. Again, the nates, the lower part of the abdomen, the inguinal region, the genitals, and the upper part of the thighs were deeply pigmented; towards the ends of the extremities, however, the pigmentation was less pronounced, with the exception of the popliteal and cubital fossæ, which were

* In cases of psoriasis, independent of the existing marks, Mueller.

† Mathieu, Pringle (1895).

‡ Barthélemy, Mackenzie, Richardière.

darker coloured. The hands were entirely free, and the face was only affected in a very slight degree. Those parts of the body which are already normally somewhat more pigmented—the genito-anal, the axillary regions, and the mammary areolæ—are often coloured very deeply, whilst the parts exposed to the light are often least marked, or remain entirely free. But, on the whole, there is no strict law for the distribution of colour. A few cases are reported* in which the hands or the face had especially shown a pronounced pigmentation. Manssurow mentions an instance in which pigmentation of the nails took place. It is not at all unusual to find at the same time the pigmented skin dry and rough, with a bran-like† desquamation and itching. In Mueller's patient urticaria factitia was present.

It is generally stated, as a distinction from Addison's disease, that in arsenical poisoning the visible mucous membranes are never pigmented. But Morrow quotes a case from Wilson in which, besides a generally diffused pigmentation, a dark colouring of the bulbus oculi was observed. A deposit of pigment in the mucous membrane of the mouth seems never to have been seen. On the other hand, Campbell, Brown, and Davis mention cases where the intestines assumed a yellowish colour, which appears not to be an infrequent occurrence in cases of arsenical poisoning. The yellowish sparkling pigment is supposed to be the product of an organic substance, and not, as previously thought, of arsenic sulphates; the connection of this pigmentation with arsenic, however, has been called in question by Mueller.

The length of time during which the pigmentation persists is very variable; generally it disappears a few weeks or months after the arsenic is stopped, especially if soon after the pigmentation shows itself. But cases are known in which it has persisted for years. In the case of our patient, where the melanosis had existed several months before the use of arsenic was discontinued, the pigmentation appeared unchanged after more than 15 months. In the ten-years-old patient of Foerster, in whom the arsenic treatment was stopped about five months after the appearance of the pig-

* Mackenzie, Guaita, quoted by Mueller, Wyss, and others.

† Resembling ichthyosis, Sederholm, Ob. V.

mentation, it had somewhat subsided after a few months, and had been reduced to patches, but the breast and the lower part of the abdomen were still coloured light brown two and a half years later. If the arsenic has been taken for many years, the pigmentation may persist during the remainder of life.* Whether age or sex are of any account in the longer or shorter duration of the pigmentation is a question which cannot be answered. The pigmentation generally disappears by becoming gradually lighter, and sometimes, as in the case of Foerster's patients, diffused areas gradually break up into patches, probably in accordance with the manner in which it commences. In a few cases the process is accompanied by slight desquamation and itching, which, in one of Moreira's patients, continued a few months after the disappearance of the pigmentation. In a few cases† the melanosis, which had partly or wholly disappeared, returned when arsenical treatment was resumed even after a long interval.

By means of the microscope‡ the pigment of arsenical melanosis has been found as granular particles in and outside the cells of the lower layer of the epithelium, as well as in the lymph spaces of the papillary layer and the lower layer of the cutis; in the latter the pigment cells were only slightly coloured.§ The brownish tint of the nails observed by Manssurow was the effect of a lemon-coloured pigmentation of the edges of the cells of the nail. The difference in intensity of colour on the various regions of the skin has been explained by differences in the number of papillæ, and the accumulation of pigment is said to be a deposit in the skin of a product of decomposition of the hæmaglobin, which is supposed to be caused by the previous destruction of the red corpuscles through the action of the arsenic.‖ The relatively infrequent appearance of pigmentation during

* Lewin; a case of Cheadle's. The persistence of the arsenical pigmentation years after the drug has been stopped finds its analogy in the pigmented marks left for a considerable time after mustard plaster, Spanish flies, &c., the cause of which is at present unknown. We once observed a pigmentation on the neck of a serotum after a well-developed suctio erotica, which remained unaltered for a whole year.

† Wyss, Sederholm, Obs. V., Foerster (1892).

‡ Wyss, Mueller.

§ Mueller.

‖ Wyss.

arsenical treatment, notwithstanding the various diseases for which it is prescribed, and the fact that the mucous membranes almost invariably remain intact, seem to us an argument against the acceptation of this theory.

The diagnosis of arsenical melanosis must be principally based on the fact that the pigmentation has developed during the use of the drug, or, in rarer cases, after accidental arsenical poisoning. At the same time, other symptoms of arsenical poisoning will probably show themselves in connection with the skin or other organs, although, as stated, the pigmentation may be the only indication of intoxication or may precede the other symptoms by a considerable time.* Neither the minute, diffused patches, which Gowers considers characteristic of the initial stage, nor the mottled appearance, which is caused by the numerous whitish spots present, can be considered a sure and constant index, for they may be observed also in pigmentation from other causes. A far more trustworthy symptom, which will serve for the diagnosis between arsenical melanosis and argyria (in which the pigmentation is rather slate-coloured), and Addison's disease, is the fact pointed out by several writers that in arsenical melanosis the visible mucous membrane is never pigmented. It is true one case has been reported, to which we have referred before, in which the bulbus oculi had been affected by pigmentation, but no case apparently where the mucous membrane of the mouth had been so affected. On the other hand, the localisation and the intensity of the pigmentation in the various regions of the skin are of no true diagnostic value owing to the uncertain course of arsenical melanosis, although the parts exposed to the light seem less easily affected than in the case of the two other diseases referred to. It is especially in respect of Addison's disease that the diagnosis may offer difficulties, and it has been proved that a comparatively large number of cases, considered to belong to this disease, were really the results of arsenical poisoning. The mistaken diagnosis was excusable because, besides the melanosis, other symptoms may occur—gastric, nervous, &c.—which are observed also in Addison's disease. It is not unlikely that similar mistakes

* Gowers.

have been made in many cases where the supra-renal bodies and the ganglia have been found healthy.* The pigmentation which sometimes appears in the cachexiæ, of tubercnlosis, cancer, malaria, &c., for which arsenic is often prescribed, may, in certain cases, have been due to the drug. With regard to the pigmentation of syphilis the diagnosis will only in very exceptional cases present any difficulties.†

For prognosis, as already pointed out, it is important to ascertain whether the arsenic has been continued for a longer or shorter time after the appearance of the pigmentation, for in the former event it is most likely that the discolouration will disappear only very slowly, or remain almost stationary. But purely individual and unknown characteristics undoubtedly play here as important a part as they do in the course of pigmentations from other causes.

The most important point in the treatment naturally is to stop the administration of arsenic. The use of diuretics, especially IK,‡ for the speedy elimination of the arsenic has also been recommended. Local treatment for the purpose of producing a superficial desquamating inflammation of the skin can hardly be expected to lead to successful results, judging from the experience gained from similar treatment for pigmentation from other causes, and it does not seem to have been attempted for arsenical melanosis.

Hutchinson (1891, who in several directions has increased our knowledge of arsenical melanosis) mentions several symptoms which would indicate the necessity for suspending the use of arsenic, namely, paræsthesia and numbness of the palms of the hands and the soles of the feet, or other regions of the skin, and general emaciation. Irritation of the conjunctiva, which is such a well-known symptom, is, according to Hutchinson, not so often present as some of the other symptoms, to which he adds: inclination to diarrhœa and extreme irritability of the bladder. To these may also be added the several arsenical dermatoses.

Keratosis palmaris and plantaris as a symptom of arsenical poisoning has only during the last few years been duly

* Rasch.

† Cf., however, a case of von Engel Reimer's quoted by Mueller.

‡ Gowers.

recognised. Although Er. Wilson had, as early as 1873, pointed out that arsenic might cause a considerable thickening of the epidermis on the surface of the hands and the feet, as also very small granulated corns, each corresponding with the opening of a sudoriferous gland, it was not until Hutchinson had published several reports on the subject in 1887 and the following years that the disease received any attention. It was then only that arsenical keratosis became a recognised disease* in France, where it had till then been ignored.† About 30 cases belonging to this class of keratosis seem to have been published, and principally from English sources. In only a minority of cases was the keratosis the sole symptom of poisoning;‡ as a rule other signs of poisoning, some slight, others more severe, were manifest either in connection with the skin or the nervous system; in about half the cases—16—the keratosis was combined with arsenical melanosis, as was observed in our patient.

Generally the keratosis developed during the treatment with arsenic of the most varied kinds of diseases, principally skin affections; in a few instances it was due to accidental poisoning with rat poison,§ or with wine containing arsenic;‖ and one patient developed keratosis from prolonged working with Schweinfurt green.¶ Arsenical keratosis, like arsenical pigmentation, varies greatly with regard to the length of time and the amount of the drug necessary for its manifestation in different patients. In acute poisoning the keratosis was observed after eleven days;§ from the ordinary medicinal use of the drug it manifested itself, at the earliest, in the course of three or four weeks; for example, in the case of a young man, aged 26 years, suffering from psoriasis, it made its appearance after a course of three weeks' subcutaneous injections of sol. arsen. nat. (eq. 10—20 gr.),** and after four weeks' treatment in a child, aged 8 years, with prurigo, who

* Besnier.
† Cf. Pringle (1891).
‡ Brooke, Crocker, Pringle (1891), Hardaway, Ludw. Nielsen (1892).
§ Moreira.
‖ Barthélemy.
¶ Gaucher and Barbe.
** Ludw. Nielsen (1892).

during that time had in all taken 10 gr. Sol. Fowleri.* Another patient had taken altogether 2½ gr. (15 cg.) ac. ars. in 29 days.† In the majority of cases, as in our patient, the keratosis only appeared after several months' use of the drug, and it even seems that it may reveal itself only after years of arsenical treatment.‡ Moreover, the keratosis generally develops so slowly that the statements of the patients as to its first appearance can be but imperfectly relied on.

Of 29 patients suffering from arsenical keratosis, 17 were men and 11 women, between the ages of 20 and 70, and fairly equally divided over the respective periods, and only one child, aged 8 years.§ In contrast with arsenical melanosis, it may be accepted that sex, and still more age, have some influence on the development of arsenical keratosis, which is explained by the fact that the skin, at least of the palms of the hands, is more exposed to "traumatisation" from labour in grown-up men than in women, and especially children.

From the published reports of arsenical keratosis it appears that the disease always manifests itself in a symmetrical manner, although it may be more strongly developed on one side than on the other. In far the largest number of cases it was found on the palms as well as on the soles, very seldom on the palms alone, and in exceptional cases exclusively on the soles.‖ It appears in two forms: either as a diffused keratosis or as numerous small scattered corns; the latter form, however, is seldom seen alone, but is generally combined with the diffused keratosis, as was the case with our patient. This combined form is met with in about the same proportion as the diffused one. In a single instance¶ small scattered corns were alone noticed on the palms, whilst the soles presented the combined form.

The diffused keratosis is usually spread over the entire flat surface of the hand and foot, as well as on the flexor

* Heuss.
† Mackenzie.
‡ Brooke, Hardaway, Mathieu, Rasch, and others.
§ Heuss.
‖ Sederholm, Obs. IX, Barthelemy, Obs. II.
¶ Payne.

surfaces and edges of the fingers and toes, but the centre of the palm, and perhaps especially the hollow part of the sole, namely, the part that is least exposed to pressure, appears to be but slightly affected or entirely free. In a few instances the keratosis has spread over the sides and backs of the feet,* or over the joints of the hand.† In one case‡ on the breast, the abdomen, and between the shoulder blades, a few patches appeared similar in nature to the affection of the hands and feet. In the case of our patient, as also in that of one previously under our observation,§ the affected skin was diffusely dry, limp, and ashen-gray coloured; the epidermis was rough and hard to the touch, and in the case of one of the patients only slightly thickened, but in the other, where the keratosis had existed for a long time, besides the isolated wart-like corns, there was a distinct diffused thickening, but apparently of the epidermis alone. The keratosis was clearly defined against the healthy part of the skin, without hyperæmic edges. These characteristics seem pretty constant in arsenical keratosis. But they allow of certain modifications; for instance, we find mention of small indentations with ragged epidermis,‖ or a roughness of the skin resembling fine shagreen.¶ In other cases† the yellowish-transparent and much thickened epidermis ($\frac{1}{8}$ in.) was somewhat softer owing to a simultaneous severe hyperidrosis. When the horny layer is very thick there may be a tendency to the formation of chaps.** The colour may, in some cases, be a grayish-brown; in one exceptional case it was coal-black.‡‡ Only Barthélemy's patients presented an erythematous border along the sides of the foot, which was the seat of a diffused plantar keratosis.

The second form of arsenical keratosis presents itself as manifold, mostly very numerous, small, more or less scattered horny excrescences.†† They are, as previously stated, seldom found alone; usually they are combined with

* Payne.
† Crocker.
‡ Mackenzie.
§ See Bibliography.
‖ Hutchinson (1888), Obs. I. and II.
¶ Rasch.
** Sederholm, Obs. IV., Mackenzie.
†† Corns, not warts. For as Hutchinson expressly says, they have no papillæ.

the diffused form of keratosis, which in most cases is strewn all over with them. In our patient the diffused keratosis is said to have developed first, the small scattered corns afterwards. These generally invade the same surfaces as those indicated above as the seat of the diffused keratosis; they may sometimes be found, like the latter, not only on the flexor part of the fingers and toes, but also on the dorsum of the hand and of the fingers and toes.* This multiple keratosis may, as Wilson pointed out, appear as minute granulated corns at the orifice of a sudorific gland;† in the case of our patient and in many others it has been impossible to verify this localisation, even with the microscope, probably because the keratosis had already entered on a more advanced stage of development. Usually these corns occur as hard, wart-like excrescences, from the size of a pin's head to that of a pea,‡ pointed or rounded in shape, and of the colour of horn, sometimes yellowish-brown, sometimes darker. In our patient they were rather flattened on the soles, and pressed deeply into the skin by walking; they had to be continually cut to prevent their getting troublesome, but speedily grew again. One exceptionally large corn under the left heel resembled exactly an ordinary cutaneous horn, rather compressed and conical, with regular longitudinal striæ; it could easily be raised slightly from the small nest-shaped hollow in the epidermis in which it had been imbedded, owing to its oblique growth from pressure during walking. As an example of the rapid growth of these corns, Heuss reports the case of one of his patients suffering from arsenical keratosis, who had a small flat corn on the dorsum of the great toe which increased in one week to the size of a hazel nut. Although several accounts are published of various diseases of the nails resulting from the use of arsenic, they seem very seldom to occur in combination with arsenical keratosis. Mathieu alone, in the case he reports, mentions that the nails had become thin and deformed.

* Pringle (1891), Fox, Payne, Moreira, and others.

† Moreira, Pringle (1891).

‡ In Payne's patients, and in one of Moreira's, the diameter varied from $\frac{1}{8}$ in. to $\frac{1}{4}$ in.

As already stated, the small keratosic growths are often observed on the orifices of the sudoriferous glands, and in the case reported by Pringle a severe hyperidrosis had also developed at the affected parts. Hutchinson mentioned on the same occasion that local hyperidrosis sometimes may be produced by arsenic, a statement which was afterwards made by Pringle. Lewin also calls attention to the increased excretion of sweat which may take place in certain circumscribed areas of the skin. In a few other cases* mention is made of a severe local hyperidrosis, which in Crocker's patient, as noticed above, caused the abundant diffused keratosis to feel soft to the touch and look yellowish-transparent. In this instance the hyperidrosis had commenced during the treatment with arsenic a few months before the keratosis. Besides, Crocker himself seemed inclined to attribute the keratosis to the hyperidrosis alone, independent of the arsenical treatment. It does not appear that increased excretion of sweat was noticed in other patients with arsenical keratosis; on the contrary, the skin was generally found rather dry.

Although arsenical keratosis usually develops imperceptibly without erythema or other inflammatory symptoms, a few exceptional instances are known, as in arsenical melanosis, in which affections of this kind preceded or followed the keratosis. (Besides, erythema and similar disturbances often occur in the soles and palms, as the effect of arsenic, without keratosis.) Brooke's patients, before the diffused keratosis appeared, complained of severe inflammation and itching of the soles; these troubles subsequently disappeared, but whenever the arsenical treatment was resumed a burning sensation was experienced at the affected spots; walking also caused pain, and there was occasional itching of the soles. Hunt† thinks that a certain tenderness of the affected parts may precede the keratosis. It has already been stated that in Barthélemy's patient an erythematous border was seen along the outer side of the foot, the seat of a plantar keratosis; after a short time the skin came away

* Crocker, Pringle (1895).

† Quoted by Morrow.

in large scales. In a few cases* where the small horny growths were found at the orifices of the sudoriferous glands,† the palms and soles were affected by an erythema which was followed by copious desquamation. A severe keratosis may cause some inconvenience in the performance of delicate manual labour and in walking, but on the whole it does not appear to produce real subjective sensations. Barthélemy (Obs. II.) mentions a case in which the sensibility of the palms and soles was greatly diminished; Hutchinson (1888) one in which feeling was lost in the right hand alone; but this was probably due to arsenical neuritis, and unconnected with the keratosis.

A few years ago—in 1885—at a time when arsenical keratosis was scarcely known, White reported two cases of epithelioma, the result of an efflorescence of psoriasis. One patient, an American doctor, aged 44, had been troubled with an obstinate psoriasis from the age of twenty-one. His skin being very sensitive, he had been almost exclusively treated with arsenic, and for many years. At the age of 34 several of the patches of psoriasis on the back of the hand, and on the lower end of the arm, changed gradually into sharply-defined, hard, horny excrescences: the same occurred on the palms. From one of these wart-like growths on the right palm cancerous ulcers developed eight years later, and in process of time the same took place on the left palm. Amputation of the lower part of the right arm and part of the left hand seemed to have effected a cure, but he died 16 months later from metastasis.‡ The second case was a man aged 52 years, who had also taken much arsenic for an obstinate psoriasis. The same wart-like excrescences appeared on the hands at the spots affected by the disease at the age of 42. One of these growths on the inside of the wrist became soft, ulcerated and developed into an epithelioma. The hands and fingers also were covered with horny, wart-like excrescences, and near the anus, on the penis, and in the inguinal folds appeared excoriated and ulcerated spots of doubtful character. The parts affected were excised,

* Wilson, quoted by Morrow, Moreira.
† Query on the volæ and plantæ?
‡ Cf. Hutchinson, 1888.

but the patient died from septic lymphangitis. The microscopical diagnosis in both cases was epithelial cancer.

The first patient went to Europe before the amputation to consult the principal medical men. He came to Hutchinson, who, in addition to the epithelioma, found the skin of the palms intensely dry, with small indentations in the horn-like epidermis, and small hard corns—in fact, a keratosis combining the diffused and the multiple types, identical with the arsenical keratosis described above. Hutchinson is perfectly right in concluding that the use of arsenic for a number of years had caused the disease, and that *this arsenical keratosis* ("*arsenical corns*") *may develop into epithelial cancer* ("*arsenical cancer*") *when the drug is not discontinued.* At the same time, as he described White's case (1888), Hutchinson reported three others of his own. A man, aged 34 years, in whose family cancer had occurred, developed, after prolonged use of arsenic for psoriasis, "corns" on the soles, the palms and the sides of the fingers. The arsenic was continued—its connection with arsenical keratosis being still unknown at that date, 1871—*and a horny excrescence of the same kind on the scrotum developed into epithelial cancer,* which was excised; at the same time the horny formations in the palms began to desquamate within a certain area. No relapse had occurred nine months later.

The second patient, for whom Hutchinson had been consulted by letter by Dr. Allbutt, was a woman, aged 25 years, who had taken a larger amount of arsenic for a pemphigus of long standing. *The skin on the palms and on the volar part of the fingers, as well as a patch behind the crista ilii was very rough*—owing, in Hutchinson's opinion, to the use of arsenic. In the latter position, and from a glandular swelling in the inguinal region, ulcerations of a cancerous nature developed (not verified microscopically), and the patient soon died. Although in both these instances the new growths did not arise from keratosis of the palms and the soles, but from wart-like excrescences on other parts of the skin (scrotum, trunk), these cases, and more especially the first, may surely, after Hutchinson, be classed in the same category as White's, for arsenical keratosis, as already stated,

has been found on other parts of the skin than the palm and the sole.

We are therefore justified in placing in the same class a case of obstinate and prolonged psoriasis, reported by H. Hebra, in which numerous patches of psoriasis on the extremities changed into epithelial, wart-like excreseences, and finally on the upper part of the arm and femur into epithelial cancer, which ended fatally. Arsenic is not mentioned in the treatment, but "various remedies" had been tried.

In Hutchinson's third patient "*corns*" *on the hands and feet* made their appearance after prolonged use of arsenic for psoriasis. They lasted for several years. At the same time the skin became dry and rough, and the sensibility of the right hand became diminished. On the great toe, where already two hard corns existed, two ulcerated patches with indurated edges, the size of a coin, were formed, which only healed after excision of the sores. As in this case by microscopical examination no elements of epithelial cancer were discovered—a fact to which Hutchinson does not attach much importance in diagnoses—it can scarcely be admitted as a case in point. It was probably a case of common arsenical ulceration.* So likewise was Gaucher and Barbe's patient, who, as the result of arsenical poisoning from prolonged working with Schweinfurt green, developed, besides a diffused keratosis on the palms and soles, deep ulcerations on the little finger and the great toe.

Finally Hutchinson mentions in the same treatise a case, reported by Cartaz, in which a cancerous ulceration of the finger arose from a patch of psoriasis. However, as nothing is said of a preceding formation of corns or of arsenical treatment—which surely must have been prescribed in the course of the disease, which had lasted 20 years—this case cannot be considered as well-authenticated evidence.†

As in the present state of our knowledge arsenic is recognised as having only an indirect influence on the development of epithelial cancer—calling into existence predisposing conditions, which by unknown processes may lead to

* Cf. Lewin, Morrow, and others.

† For the sake of completeness it may be stated that one more case of epithelioma of the foot in a patient with psoriasis has been mentioned by Pozzi

the formation of cancer—Hutchinson's definition of "arsenical corns" can only in this sense be considered correct. As is well known, various chronic affections—old ulcerations, lupus, &c.—especially when they have been the consequence of repeated inflammations, may become the seat of a cancerous infiltration (query: from infection); so also may the wart-like formations, and especially the corns. Lebert, who collected all the cases of corns published up to 1864—109 in number—found that 127 of them were connected with epithelioma. The same proportion may safely be accepted for the cases of arsenical keratosis complicated with epithelioma, because these "arsenical corns"—and it is only this form of arsenical keratosis which has been found complicated with epithelioma—which have not yet been studied in their histology, are undoubtedly very nearly connected, if not perfectly identical, with the ordinary kind of corns. Moreover, as stated above, one of the small horny formations on the sole of our patient was, clinically, only a well-developed corn, with its regular longitudinal striæ.

If the arsenical treatment is continued after the keratosis has formed carcinoma may be the sequel, but only in very exceptional cases. As a rule, the keratosis, after having reached a certain point, remains stationary. In only a few cases the course of the keratosis, after the discontinuing of the arsenic, is described. In most of them the keratosis disappeared spontaneously, or after suitable local treatment, in a few weeks, months, or longer.* In the case of our patient, where the keratosis had remained unaltered $1\frac{1}{4}$ year after the arsenic had been stopped, it quickly subsided after local

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(cf. Kaposi-Besnier and Doyon's Handbook, 1891, I., p. 558, note). As we could not refer to the original we can give no details as to the development of the new growth. Another case is mentioned by Lane of a sexagenarian with psoriasis, who, having been treated with arsenic for 30 years, showed eleven distinct epitheliomata on the lower arm, the scrotum, and the perineum; only a single one of these growths could possibly have been developed from a patch of psoriasis. As it does not seem that the formation of the epitheliomata had been preceded by arsenical keratosis, this case can scarcely be taken into account. During the discussion on this case Hulke mentioned that he had tried to obtain statistics of similar excrescences among the miners in the arsenic mines of Cornwall, but with negative results.

* Moreira, Heuss Rasch, Sederholm, Obs. IV., IX.

treatment, but the ultimate result is not known. In Fox's case, where the keratosis had persisted for about four years, a radical cure was effected by salicyl plasters. On the other hand, in one of Pringle's cases, where the keratosis had only existed a few months, the cessation of the drug and the use of preparations of salicyl and resorcin only afforded temporary relief, and the keratosis returned as soon as the remedies were suspended.

The histology and pathogenesis of arsenical keratosis are still unknown. Lewin's opinion that arsenical dermatoses generally arise from the direct action of the arsenic on the skin, through the glands of which it is excreted—as well as through the kidneys and the salivary glands, &c.—agrees with the hypothesis that the small arsenical keratoses originate at the orifices of the sudoriferous glands, as well as with the fact that the keratosis has sometimes, though rarely, been preceded or accompanied by a local hyperidrosis. Other writers consider arsenical keratosis a tropho-neurotic disease, because the use of arsenic often gives rise to nervous affections. In this way the keratosis of Gaucher and Barbe's patient may be accounted for, although the poisoning took place from without—through working with Schweinfurt green—because at the same time a sclerodachyle was developed. Moreover, Besnier's description of a form of his "Kératodermie symétrique des extrémités,"* which he also considers a tropho-neurotic affection, agrees exactly with that form of arsenical keratosis which makes its appearance in multiple small foci; so that probably in this form some cases of arsenical keratosis may have been included, for, as stated before, the disease was not recognised in France.

For the present at least, it is impossible to give any definite clinical signs by which arsenical may be distinguished from keratoses from other causes, more especially as it has only been recognised as a distinct form within the last ten years. The diagnosis, therefore, must be principally based on the fact that it is an acquired—not a congenital or hereditary—symmetrically developed keratosis, that it has the localisation and clinical character described above, that it

* En foyers: cf. Kaposi-Besnier and Doyon's Manual, 1891, II., p. 43, note.

develops during arsenical treatment or through accidental poisoning with that drug, and is generally accompanied by other symptoms of arsenical poisoning.

With regard to the prognosis, we can only repeat what has been stated before. Judging from the data we have, we may safely conclude that, as soon as the arsenical treatment is discontinued, the keratosis will disappear, either spontaneously or after suitable local treatment. But it is quite possible that the affection may prove obstinate and persistent. In very exceptional cases it may be the commencement of the formation of epithelioma.

After the drug has been suspended, the usual remedies for keratoses will be found effectual: they consist of warm soap and soda baths, poultices, india-rubber gloves, &c., and other remedies for corns, emplastrum saponal, salicyl, or other strong preparations of salicyl and resorcin.

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EPITHELIOMA

AS A

SEQUEL OF PSORIASIS

AND THE

PROBABILITY OF ITS ARSENICAL ORIGIN.

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EPITHELIOMA AS A SEQUEL OF PSORIASIS AND THE PROBABILITY OF ITS ARSENICAL ORIGIN.*

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In November, 1898, Miss M., aged thirty-five years, came under my professional care through the kindness of Dr. H. W. Stelwagon, whose patient she had been for many years, but who no longer found it convenient to look after her. At that time she presented the following lesions: On the outer side of the heel of the left foot was an ulcer about two inches in diameter, shallow at the edges but quite deep in the centre, with a perfectly flat, uninfiltrated border. Close by this large ulcer, which was very painful, was a much smaller, very superficial one, which was evidently undergoing cicatrization. In addition to these ulcerative lesions the soles of both feet were the seat of a marked keratosis, which existed as diffuse patches upon the heels, and shot- to pea-sized, clavus-like elevations, most numerous beneath the metatarso-phalangeal articulations. The palms of both hands were also the seat of a keratosis even more marked than the soles, the palmar surface of the fingers presenting numerous shot-sized, corneous elevations, while the centre of the palms was dry and thickened. Besides these keratosic lesions there were several small, superficial ulcers upon the palmar surface of the fingers, which had originated at the site of corns and were quite painful. Upon the elbows and trunk were a few patches of psoriasis, which presented nothing unusual. Upon the left breast was an irregularly oval, quarter-dollar-sized, red, somewhat thickened, slightly crusted patch, which was just beginning to ulcerate in small areas. In the left groin was a bosselated tumour the size of a small orange, firm and elastic, except upon the summit, where the skin was evidently upon the point of giving way. The his-

* Read at the twenty-third annual meeting of the American Dermatological Association, May 30, 1899.

tory of the case, as obtained from Dr. Stelwagon, and the statements of the patient herself, were as follows: At fourteen years of age she began to have psoriasis of the ordinary type, from which she had never been entirely free since, and for which she had taken arsenic in considerable doses over long periods of time. Some nine or ten years after the first appearance of the psoriasis horny patches and corn-like elevations began to appear in the palms of the hands and on the soles of the feet, and at a still later period—how soon after the keratosis I was not able to learn accurately—small, superficial ulcers occurred beneath these horny masses, which obstinately refused to heal under any kind of treatment. At this time an ulcer appeared upon the left heel, near the site of the one above described, which, after being treated in vain with various local applications, was thoroughly curetted by her medical attendant and healed entirely. One year later a new one appeared, which slowly but steadily extended until the patient's death, uninfluenced in its progress by treatment. Seven months before the date of my first visit the tumour in the groin began, and this steadily, at first slowly, but later more rapidly, grew larger. The history from this time on can, unfortunately, be told in a very few words. The tumour in the groin speedily ulcerated, forming a deep, fungating, foul ulcer, which discharged very abundantly. This was soon followed by more or less continuous fever, loss of appetite, rapid emaciation, and death about two months after my first visit. During the short period the patient was under my observation the large ulcer upon the heel underwent but little change, but the one alongside of it, and another upon the palmar surface of the middle finger of the left hand, which was unusually painful, were completely cicatrized some little time before death occurred, both having lasted many months. The few patches of psoriasis present at an earlier period also completely disappeared. Soon after taking charge of the case I excised a small portion of the margin of the ulcer upon the heel, and submitted it to microscopical examination. This fully established the carcinomatous character of the lesion. There were many well-defined, slender, branching tracts of epithelial cells extending well down into the corium, a considerable number of epithelial cell-nests, and a scanty infiltration of round cells. Sections

of the secondary tumour in the groin, made after death, showed it to be composed of epithelial cells contained in thin-walled alveoli. While I think we may assume that all the ulcerative lesions were of the same character, I regret that this was not established beyond doubt by sections of the smaller ones; but this precaution was in some manner overlooked.

To sum up the leading features of this very interesting case, we have a psoriasis, first, of the ordinary kind, lasting many years, for which arsenic was taken in considerable doses for long periods; after a time keratosis of a peculiar type upon the palms and soles, characterized by the formation of clavus-like elevations; and, finally, epithelioma at the site of several of these corneous lesions, followed by a metastatic growth in the groin, causing the death of the patient.

The first case of epithelioma associated with psoriasis of which I have been able to find any record was reported by Pozzi* in 1874. The patient was a man, aged forty-five years, who had suffered twenty-five years from confluent psoriasis. There was also psoriasis of the nails, with considerable hypertrophy of the subungual derma. The epithelioma, which was of very slow evolution, began as a small excoriation upon the foot five years after the appearance of the psoriasis. In addition to the hypertrophy of the nails, already alluded to, there were epidermic warts.

A few years later Cartaz† reported a second case. A man, aged forty years, had had psoriasis twenty-three years, first appearing upon the elbows, then upon the soles of the feet, and, finally, upon different parts of the body. Upon the palms and soles the psoriasis had produced verrucose scales, varying in size from a pin-head to a lentil. In consequence of repeated scratching of one of these warty elevations upon the palmar surface of the right ring finger it was torn away, producing an ulcer which, instead of healing, gradually enlarged. A diagnosis of "cancroïde" was made, and amputation performed. In neither of these two cases is any mention made of the kind of treatment employed, if any, against the psoriasis.

* Bulletin de la Société Anatomique de Paris, 1874.
† Bulletin de la Société Anatomique de Paris, 1877.

In 1885 a distinguished member of this Association, Dr. J. C. White, reported two cases of long-standing psoriasis, followed by wart-like growths, which terminated in carcinoma.* In the first of these the patient was a man in whom psoriasis began at twenty-one years of age, and was constantly present from that time on in a greater or less degree, notwithstanding treatment by Fowler's and Donovan's solutions. After about fifteen years' duration several of the psoriatic patches began to undergo keratosic change, being finally converted into outgrowths like callosities or some form of wart. Some years later one of these wart-like outgrowths, seated upon the right palm, and another upon the left, began to ulcerate, and in spite of various applications, cauterization, and scraping, gradually grew larger. Finally, as a last resort, the right hand and the fore and middle fingers of the left were amputated. A microscopical examination established the diagnosis of cancer. The second patient was also a man, aged fifty-two years, who had suffered from psoriasis since early manhood, for which various methods of treatment had been tried, including arsenic. At about forty years of age several of the patches of psoriasis upon the hands became thickened and horny in appearance, and were finally transformed into warty outgrowths, one of which, upon the palmar surface of the wrist, softening, formed an ulcer two by one and a half inches, which refused to heal in spite of repeated cauterizations and scrapings. There was also a warty formation, which was beginning to soften, between the fingers. There was a small ulcerating patch upon the buttocks and two small crusted excoriations upon the penis and in the groin respectively. The diseased tissues were thoroughly excised, and healing was progressing favourably, when a deep cellulitis of the axilla, accompanied by grave constitutional symptoms, suddenly developed, causing the death of the patient. In this case, as in the preceding one, the clinical diagnosis of cancer was confirmed by the microscopical examination.

In 1887, at a meeting of the Pathological Society of London, Mr. Jonathan Hutchinson† reported three cases of psoriasis which terminated in carcinoma; but one of these, as

* American Journal of the Medical Sciences, Vol. LXXXIX.

† British Medical Journal, December 10, 1887.

it appeared later, was the first case, already reported by Dr. White. Mr. Hutchinson's first case occurred in a man whose psoriasis had lasted for many years, and for which he had taken arsenic. A corn, after a time, appeared upon the sole of the foot, which ulcerated, and the ulcer continuing to enlarge in spite of treatment, it was excised. A microscopical examination of the excised lesion was inconclusive as to its nature. Small corns had also developed upon the palms of the hands. The third case was also a man, aged thirty-four years, with a long-standing psoriasis, for which he had been treated with arsenic for a long time. Small corns were scattered over the palms and soles. After a time epithelial cancer of the scrotum developed. To these cases he has recently added another.* The patient was a man, aged forty-six years, who had suffered from psoriasis from boyhood, for which he had taken liberal quantities of arsenic for many years. After a time cancerous ulceration of two patches of psoriasis, one on the abdomen, the other on the back, developed, and this was followed by a glandular growth in the groin, which ulcerated, forming a large excavation. The patient finally died from exhaustion. Although the palms were harsh and dry no actual keratosis was present.

Hans Hebra† has reported a case of multiple epitheliomatous lesions occurring in a man who had been the subject of psoriasis for many years. The psoriasis, which at first did not differ from the ordinary type, after a time assumed a warty character, requiring mechanical means to remove the epithelial deposits. Three years after the patient was first seen the warty excrescences split up, causing fissures and deep losses of substance. Ulcers appeared upon the arm and thigh which refused to heal. One of these upon the thigh was excised, but soon returned. Fever and rapid loss of strength ensued, and the case terminated fatally. No details as to the treatment of the psoriasis are given. Examination of the excised parts demonstrated the epitheliomatous character of the ulcers.

Arbuthnot Lane‡ has also reported a case of multiple epithelioma occurring in a psoriatic man, aged sixty years.

* Archives of Surgery, 1898.

† Monatshefte f. praktische Dermatologie, January, 1887.

‡ British Medical Journal, February 9, 1894.

who had taken arsenic for thirty years. On the forearm was an ulcerating epithelioma two inches in diameter. This was removed, but one year later three separate epithelial growths appeared upon the serotum and perineum, and these were soon followed by two other raised plaques in the same locality. These lesions were excised and found to be epitheliomatous. A month or two later two new typical epithelioma were removed from the scrotum. Altogether the patient had eleven separate foci of malignant growths—four on the forearm, seven on the scrotum and perineum—but in only one, near the anus, did the growth seem to arise in a patch of psoriasis.

Geyer,* in the very extensive bibliography appended to a recent paper upon the chronic changes induced in the skin by arsenic, refers to a case of carcinoma of the hands arising from a plaque of psoriasis, reported by Power. Beyond the statement that the case was regarded as one of cancer, probably due to arsenic, no details are given, and I have been unable, to my great regret, to find the original report, although it was diligently searched for.

These ten cases, which, after a careful search, I believe comprise all thus far reported, together with my own, present a remarkable uniformity in their clinical features and course. In all of them the psoriasis, which at first presented the ordinary type of eruption, was of long standing, usually many years; in all but three some form of keratosis was a marked feature, appearing, after a variable period, most frequently upon the palms and soles in the shape of corn-like excrescences, and finally cancerous ulceration, beginning beneath one or more of these horny excrescences, occurred. In all in which any mention is made of the treatment of the psoriasis—eight out of the eleven—arsenic had been given in considerable quantity for a long period; and, in view of its almost universal use in this malady, its administration in the remaining three cannot be positively excluded. It deserves special notice, that in a large proportion of the cases—50 per cent.—the cancerous ulceration appeared before forty years of age—in one, that of Pozzi, as early as twenty-five—and it is also remarkable that in the same large proportion—50 per cent.—the ulcerative lesion was multiple. The early appear-

* Archiv. f. Derm. und Syph., Bd. XLIII.

ance and multiple character of the carcinoma accompanying psoriasis would seem to point to some special etiological factor.

While the whole number of cases is a small one, yet it is too large to permit the assumption that the association of these two diseases was entirely an accidental one. When Mr. Hutchinson reported the two cases referred to above, it was in support of the statement made by him that arsenic given in large doses for a considerable time might produce a form of epithelial cancer. Upon the same occasion he referred to a case, communicated to him by Allbutt, in which a young lady who had taken arsenic for many years for pemphigus, with only occasional remissions, after a time developed an ulcer upon the crest of the ilium. Following the development of this ulcer the glands enlarged and a tumour appeared upon the thigh, causing the patient's death at twenty-five years, an extremely early age for death from carcinoma. Some years later he reported another case, under his own observation,* in which a man, aged thirty-five years, became the subject of keratosis of the palms, which was followed by cancer of the palm and scrotum. This patient had taken considerable quantities of arsenic for acne. It should be noted, too, that the ulcerative lesions were multiple.

But prior to these observations of Hutchinson, Hardy† declared that he had seen cancer develop frequently enough in those affected with psoriasis to believe in a certain connection between the two maladies, and he quoted Bazin as holding the same opinion. Nielsen, on the other hand, although he saw a cancer of the breast develop in one of his cases, found the two affections so rarely associated in his experience that he could trace no connection between them.‡

So long ago as 1851 Romberg§ described an affection of the palms and soles characterized by epidermic desquamation, due to the internal use of arsenic. At a later period Erasmus Wilson‖ called attention to the fact that not only desquamation of the palms and soles might be produced in this way, but also thickening of the epidermis and the formation of small

* Archives of Surgery, Vol. V.

† Traité des Maladies de la Peau.

‡ Selected Monographs on Dermatology, New Sydenham Society.

§ Klinische Wahrnehmungen und Beobachtungen.

‖ Lectures on Dermatology, 1873.

"corns," the latter being seated at the mouths of the sweat-ducts. Within recent years a considerable number of cases of palmar keratosis due to arsenic have been reported by trustworthy observers, such as Hutchinson, Colcott, Fox, Crocker, Malcolm Morris, Pringle, Hardaway and others. In these cases the arsenic had been taken for such a variety of dissimilar affections, such as acne, pemphigus, lichen planus, laryngitis, epilepsy, sarcoma, psoriasis, that the keratosis could in no way be regarded as the consequence of the disease; or it had been introduced into the system accidentally, producing, besides the keratosis, other symptoms of arsenical poisoning. In the greater number there were shot- to pea-sized firm elevations resembling the ordinary corn. Now, it is a very suggestive fact, that in eight out of the eleven cases of psoriasis followed by epithelioma some form of keratosis preceded for a greater or less period the appearance of the cancerous lesion, and in seven this keratosis was of the palmar and plantar variety, such as is found in the majority of cases due to arsenic. Certainly, this fact lends strong support to the view that the carcinoma may also be of arsenical origin.

In discussing the report of Lane's case, referred to above, Mr. Hulke, the then President of the Clinical Society of London, remarked that he had made inquiries among the workers in the mines of Cornwall, who are exposed to the inhalation of arsenic vapours, as to the occurrence of such growths among them, but he had not been able to learn of any; and Mr. Butlin,* who at another time had made a somewhat similar inquiry among smelters exposed to arsenic fumes, did not find that such workers were especially liable to carcinoma, particularly of the scrotum, as had been asserted. But this negative evidence is, in my opinion, more than offset by the statement recently made by Geyer, in the paper already referred to, that among the inhabitants of Reichenstein, a small town in Prussia, where arsenic mining is carried on, carcinoma, having its beginning in "arsenic warts" on the fingers, is frequently observed. And it is especially significant, that beside other evidences of arsenic-poisoning, such as melanosis and cachexia, diffused and

* Three Lectures on Cancer of the Scrotum in Chimney-sweepers and others. British Medical Journal, 1892.

circumscribed keratosis of the palms occurs in these cases, six such being referred to in a communication made to Geyer by physicians resident in the place.

Conclusions drawn from so small a number of cases cannot be considered as final, but the evidence thus far in our possession is, I think, of such a character as to permit us to accept as very probable, at least, the arsenical origin of the epithelioma in these cases.

In concluding, I wish particularly to call attention to the very great importance of this subject in connection with recent theories concerning the pathogenesis of carcinoma in general. If it can be shown that the internal administration of arsenic is capable of producing carcinoma, we must either abandon all theories as to the parasitic origin of this grave malady, or we must assume the multiple character of the agents capable of producing it.

LICHEN SCROFULOSORUM IN A NEGRO.

BY

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LICHEN SCROFULOSORUM IN A NEGRO.

By T. Caspar Gilchrist, M.R.C.S., L.S.A.

This case is of interest not only on account of its great rarity in this country, only four cases having been previously reported, but also because it is the first recorded instance in the negro. In the four cases already reported, one of which occurred in Canada, no microscopial examination was made.

While attending a number of negro children in an orphan asylum for tinea tonsurans, one young girl, eleven years of age, was brought to me with some lesions on the back and thighs which the attendant thought were ringworm patches and which had been noticed a few days previously. The patient appeared to be a healthy, well-nourished girl; she was not anæmic, did not complain of anything, had a good appetite but was rather quiet in her manner. The tongue was clean. On examination there were found on the upper portion of the back a number of round and oval patches varying from about 10 to 20 mm. in diameter. A few similar patches were found on the extensor surfaces of both thighs, about the left groin, on the anterior surface of the right thigh and in the pubic region. The patches all consisted of groups of small, conical, slightly scaly and therefore whitish firm papules, each papule being about 0.5 mm. in diameter, raised and presenting a flattened summit which was covered with a somewhat adherent but not profuse whitish scale, on removal of which a bleeding surface was exposed. The papules presented in every patch exactly the same character and were always discrete and of the same size. There was a slight red areola surrounding the base of the papules. The most recent patch presented a group of seven rather closely aggregated conical papules which were not scaly. The oldest groups which were in the groin were much larger and the central portion appeared to be clearing up, although on close examination one could still detect the remains of slightly scaling papules which were

much flattened. Many of the lesions were pierced by lanugo hairs and were therefore situated around hair follicles. Two patches on the left groin were becoming confluent and thus formed an irregularly shaped area.

This case was not diagnosed absolutely at first, and numerous scales were examined in the usual way for the ringworm fungus but no evidence of any mycelium or spores could be found. The patient was seen every other day and numerous new lesions were observed developing, especially on the back as well as on the abdomen, forearms, and arms. Five weeks after the first appearance of the eruption a typical phlyctenular conjunctivitis of the right eye developed. The diagnosis was confirmed by Dr. Theobald. The distribution of the lesions at this time was as follows: A few scattered patches on the extensor surfaces of the forearms and arms; 4 patches on the right side of the chest; 5 scattered areas on the abdomen between the umbilicus and pubes; nearly 60 groups distributed over the whole back; a few extensive patches on the extensor surfaces of both thighs and numerous areas in both groins. The head, neck, hands, legs, and feet were all clear.

Patches which were only two days old were seen to consist of from four to seven, conical but flattened, firm, non-scaly papules, some arranged around, others between the hair follicles. Many of the lesions presented the appearance of a keratosis pilaris. The papules always appeared in the same way, gradually developing whitish, but not profuse, adherent scales, on removal of which a bleeding surface was exposed. The patches were gradually increased in size by the addition of new papules around the periphery while the older central lesion gradually flattened but remained scaly. The lesions then assumed a circular or oval-shaped aspect with a cleared-up centre. The long axis of the patches in the lumbar region was transverse to the body. When two adjoining patches approached one another the intervening papules showed a tendency to gradually disappear, but over the region of the right scapula there was a large irregular area of papules, which was made up of 10 groups, none of which had cleared up in the centre. A whitish collarette extended up the hairs in many of the papules in the lumbar region. No vesicles or pustules were observed clinically during the course of the

disease. A few solitary papules could be detected scattered over the back. All varieties of the lesions are well shown in the photograph (Fig. I) especially if a hand magnifier be used. There were no subjective symptoms.

A probable diagnosis of lichen scrofulosorum was made at first which was confirmed by the extension of the lesions, their uniform character and the appearance of a typical phlyctenular conjunctivitis. Numerous enlarged lymphatic glands were also present, but as they occur often in healthy negroes, this symptom was not regarded as important.

The patient is the fifth of eight children (five girls and three boys), all living and in good health with the exception of one girl who died of "consumption." The father and mother are living and in good health. There is no tuberculosis in any form in the family now living.

Under the internal administration of hypophosphites and cod liver oil the cutaneous and eye troubles both rapidly disappeared. The sections all presented two striking features: (1) semiglobular-looking masses situated in the horny layer and in the majority of instances around the hair follicles, and (2) marked pathological changes in the upper portion of the corium beneath these papular masses and also around the hair follicles, especially the deepest portion. The latter was characterized by its tubercular structure. One could follow in the sections the formation of these clinical papules. Fig. II. explains their genesis. The blood-vessels in the upper portion of the corium and papillæ were dilated and many polynuclear leucocytes had wandered out into the tissue and into the epidermis up to the horny layer where these cells became disintegrated; numerous lymphoid cells were found in the same situation, undergoing the same processes. Thus a mass of detritus and an apparent firm ground substance is deposited in the horny layer. This ground substance takes up the eosin stain very readily while the cells take up the hæmatoxylin. There are also a few degenerated epithelial cells in the mass of detritus. The stratum lucidum and stratum granulosum have disappeared. No apparent fluid exudation accompanies this emigration of cells through the rete, and the epidermal cells are but little swollen, nor are the interepithelial spaces much widened. Large numbers of

pigment granules are also scattered throughout the papular lesion

In Fig. III. is represented a section of the whole patch excised showing three papules (P), all of which are well marked. One shows its relation to a hair follicle (P); from the second it is evident that the section has just passed outside of the follicular opening as evidenced by the presence of the lower portion of the follicle (H); while the connection of the third with a hair follicle is seen in another section. The more pronounced papules show that they are made up of the same materials which have already been described, with the exception that there is a larger amount of pigment in the lesions. Directly in contact with the hair (H) there is a well-marked hyperkeratosis encircled by the papular lesions. This hyperkeratosis extends nearly half way down to the hair follicle. The middle papule exhibits completely the nature of the lesion just outside of the hair; it consists of a firm substance imbedded in which are enormous numbers of degenerated polynuclear leucocytes, lymphoid cells, many epithelial cells and masses of pigment granules. The mucous layer beneath consists of two layers of cells through which are emigrating hundreds of wandering cells. There is some widening of the interepithelial spaces, but no marked œdema. The corium, especially directly beneath the papules and around the hair follicles, shows marked changes. In the first region there is a fairly well-defined area consisting of the papillæ and upper portion of the corium, in which are massed large numbers of lymphoid cells, numerous polynuclear leucocytes and some plasma cells with dilated blood-vessels. (Fig. III., C.)

Around the hair follicles in the lower portion are masses of chiefly round mononuclear cells, some plasma cells and epithelioid cells and a few mast cells. In four sections typical tubercles were observed in this situation (Fig. III., G), with giant cells forming the centre surrounded by numerous epithelioid cells and mononuclear round cells at the periphery. The hair follicles themselves are unaffected. The blood-vessels (V) throughout the corium are dilated, are surrounded by numerous mononuclear round cells, a few plasma cells and numbers of polynuclear leucocytes. Two unaffected sebaceous glands were seen in one of the sections. The sweat

ducts and sweat glands were normal, although a duct was seen passing close to the lesion. The blood-vessels accompanying the sweat duct were dilated and surrounded by additional cells as were other vessels. No tubercle bacilli were found in any of the sections stained for this purpose.

Hebra first described the disease and named it lichen scrofulosorum to characterize its clinical features. He declared that it was always accompanied by other symptoms of scrofula. The disease had been previously described as lichen simplex by Erasmus Wilson, and as lichen circumscriptus by Cazenave. Jacobi in 1891 drew attention to the tubercular nature of the lesions, which he thought to be a perifollicular tuberculosis of the skin. Although he demonstrated a single tubercle bacillus in one of his sections, an inoculation into guinea-pigs gave negative results. Later (1896) he demonstrated the presence of tubercle bacilli in a typical case and obtained positive results in a rabbit. In 1892 Sack decided, after a careful histological examination, that the disease was a miliary tuberculosis of the skin, the nodules showing a central caseation, then giant cells, epithelioid cells and small round cells. He suggested "tuberculosis lichenoides cutis" as a more applicable title. Later observers have apparently demonstrated the tuberculous nature of the affection, especially of the severer forms. Thus Jadassohn found in 19 cases 14 associated with tuberculosis, and only one case in which no such disease was present. He was of the opinion that the disease was non-bacillary, but that it was a disease of tuberculous persons. Of 16 cases treated with tuberculin 14 reacted typically, but although inoculations were made into guinea-pigs from nine of the cases, negative results followed. Kaposi believes that there is nothing to prove that lichen scrofulosorum is a manifestation of tuberculosis, although he asserts that tuberculosis is always present. In Tilbury Fox's six cases he noted the presence of tuberculous symptoms in the patients. Pellizarri succeeded in producing tuberculosis in a guinea-pig after the inoculation from one case.

Haushalter (1898) inoculated 4 guinea-pigs from 2 cases and they became infected with tuberculosis, one of the cases had an otitis media, the other a tuberculous lymph gland as well as enlargement of other cervical glands. Some German dermatologists, *e.g.*, Kromayer, Kaposi and Lukasiewicz, are

opposed to the tubercular origin of this disease on account of the absence of caseation, the mildness of the affection and the rapid recovery. Only a very few cases have been recorded in France, and in those examined histologically no tubercle bacilli were ever demonstrated, although the subjects were tuberculous. It was believed, therefore, by the French dermatologists, Hallopeau, Brocq, and Bureau, that the lesions of lichen scrofulosorum were not due to direct infection but rather to the toxin of tuberculosis. Hallopeau reported one case which was associated with lupus. The lichen eruption was scattered chiefly over the trunk, but one group of papules was situated directly around the lupus nodule which had a scar in the centre. In Lefebre's case no bacilli were found in the sections, and the animal inoculation was negative. In both the cases recorded by Morris and Crocker tuberculous glands were present, but in Walker's case tuberculosis in any form was absent, neither was there any tuberculous history.

With reference to the American reports, only two cases have been exhibited at the meetings of Societies, and of these only clinical histories have been given. In all the cases recorded, the histological findings always show a likeness to those in tuberculosis, but in most instances after diligent search no bacilli have been found, nor was the disease reproduced in guinea-pigs after inoculation. The inoculations, however, which have resulted successfully, have demonstrated its tuberculous nature in those cases. My own case is a comparatively mild one and the presence of bacilli could not be demonstrated. Clinically it presents all the typical features of a lichen scrofulosorum as originally described by Hebra with the exception of the colour, which would naturally differ in a negro's skin. Tilbury Fox called attention to the fact that instead of always appearing in groups, the papules may occur singly.

Sack in his descriptions and drawings shows that the papule is formed by the miliary tubercle being deposited directly beneath the epidermis and by some slight hyperkeratosis of the horny layer.

In my case the papules consist of distinct lesions involving the horny layer, and form, as it were, a dry pustule. It was neither clinically nor histologically a pustule, since it appeared to be made up of a homogeneous ground substance

with masses of nuclear detritus and numerous pigment granules. There was no special hyperkeratosis. The tubercular nature of the disease was far from being pronounced histologically in the present case and the tubercles were situated around the lower portion of the hair follicle.

It is strange that a tubercular cutaneous eruption which yielded so readily to cod-liver oil should arise in a well-fed, healthy child with good hygienic surroundings and without previous history of tuberculosis. Clinically the case suggests the adoption of Hebra's title of lichen scrofulosorum or Unna's folliculitis scrofulosorum rather than tuberculosis follicularis. Since successful inoculations, however, have been made in at least three cases, then the latter title would be more correct.

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FIG. I.—Photograph of a case of lichen scrofulosorum in a negro girl. The lesion can be best seen by using a hand magnifier as a small scaly papular eruption.

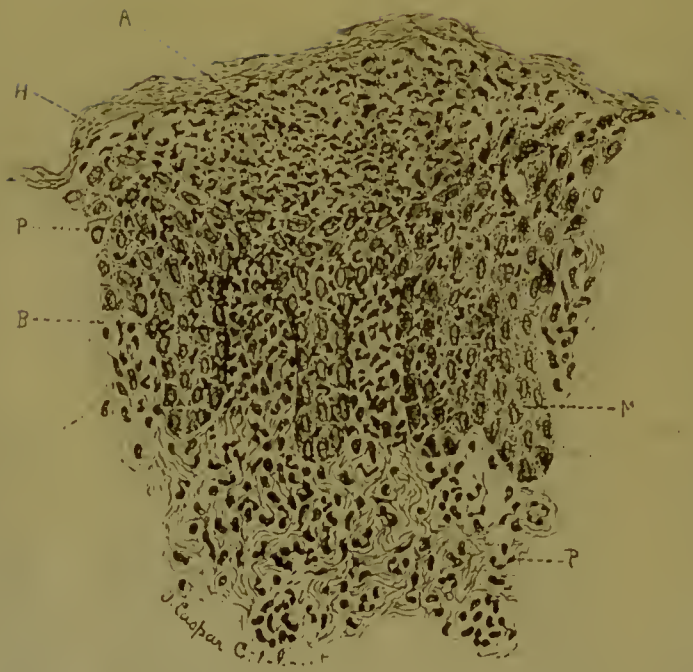

FIG. II.—Shows a commencing papule (A) which is formed between the horny layer (H) and the mucous layers (M). Numerous polynuclear leucocytes (P) and lymphoid cells are emigrating through the epidermis to the horny layer. Two papillæ (B) are filled with wandering cells and dilated vessels.

FIG. III.—Shows three well marked papules (P, P, P): one encircles a hair (H); in the other two the section has passed outside the follicular opening. H, H, are hair follicles; C, collections of lymphoid, plasma and connective-tissue cells, and polynuclear leucocytes; V, V, dilated blood-vessels; G, is a tubercle near the lower portion of the hair follicle H; F, is fat; S, sweat glands; D, collection of cells round hair follicle.

THE

NATURE OF LUPUS ERYTHEMATOSUS.

BY

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THE NATURE OF LUPUS ERYTHEMATOSUS.

By C. P. M. Boeck, M.D.

Since the meeting of the International Medical Congress in 1881 this very strange and peculiar disease has been a standing subject for reports and discussion by dermatologists at almost all their meetings and congresses. In spite of this there remain not only many interesting questions still unsettled as to the clinical forms and the pathology of the disease, but the question of its etiology has above all gained special interest, for the number of those who hold that lupus erythematosus has an intimate connection with tuberculosis, that most murderous of all diseases at the present time, at least amongst civilised nations, is steadily increasing.

In my opinion it is clear that lupus erythematosus is one of the links in the whole series of affections of the skin which all point back to tuberculosis as their common source of origin. Such a group was, it will be remembered, formed by M. Hallopeau at the Dermatological Congress in London two years ago.

It will be convenient here to include under the term "lupus erythematosus" only such forms as are so-called by all, that is to say, all the common discoid forms. I shall draw no distinction between the deeply infiltrated and the more inconstant and transient forms, since in my experience a successive transition from the most inconstant, for instance, erythema lupinosum (Veiel), to the most persistent forms may easily be traced. They are all of eruptive inflammatory nature. The most persistent and infiltrated patches are at one time more red and inflamed, at another time more pale, and the conditions are thus kept up through a continued series of eruptions. The very rare, more generalised, and more malignant form, the lupus erythematosus disseminatus et aggregatus described by Kaposi, is also unanimously acknowledged to be a form of lupus erythematosus.

The theory that lupus erythematosus is of tuberculous origin, an opinion which Mr. Jonathan Hutchinson was one of the first to maintain, is adopted also by some of the leading men of the French Dermatological School, especially M. Besnier. At the Dermatological Congress in 1892 Dr. Jamieson supported the theory of the tuberculous origin of the disease, but suggested an angeio-neurotic pathogenesis for it. According to M. Hallopeau, most French dermatologists have recently adopted the theory of the tuberculous nature of the disease. Mr. Hutchinson, M. Besnier, and his colleagues were led to infer the tuberculous nature of lupus erythematosus from clinical observation, and at the present time this seems to be the only basis for investigation. Microscopical, bacteriological, and experimental researches have, as a rule, failed to give positive results. The only reservation to be made is with regard to microscopical investigation, as will be pointed out later. Injections of tuberculin have not given a positive answer, and more is to be hoped for from clinical and statistical investigation.

Statistics.

My own statistics give, in my opinion, an answer sufficiently positive in favour of the existence of a decided connection between this disease and tuberculosis, so also do the French statistics as stated by M. Hallopeau in a recent paper in the "Semaine Médicale." I have collected from my own practice in recent years 42 cases of the common form of lupus erythematosus. Of these 42 cases, which were not selected, 35 were females and 7 males.

The age of the patients at the onset of the disease was noted in 29 cases; the average was found to be 32 years. Three of the patients were children, and in the youngest of them the disease began at 5 years. The most advanced age at which the disease began was 62 years. This patient was a man. The oldest patient observed was a man aged 64 years. Kaposi has seen the disease as early as 3 years of age, and he adds that he saw it once in "a very old individual." Some months ago Mr. Malcolm Morris demonstrated at the Dermatological Society of London a case in a woman, aged 72; nevertheless, it is, as is well known, rare to find old people suffering from

this disease. Whatever may be the explanation of this fact I have frequently observed that when lupus erythematosus is beginning to fade away in elderly persons they themselves suddenly begin to shrink and decay. I have not yet had the opportunity of following up these cases to the end, but it is the general opinion of French writers that these patients very frequently succumb to pulmonary tuberculosis, but it would be of the greatest importance to collect well-established facts bearing on this point.

The Possible Connection of Lupus Erythematosus with Tuberculosis.

Of my 42 cases 28, or exactly two-thirds, presented evident symptoms of present or past tuberculosis, no less than 23, that is, almost 55 per cent., presented evident tuberculous swollen glands and scars produced by suppuration of glands in the neck, 8 patients presented traces of scrofulous affections of the cornea, and 2 patients had been operated upon for severe tuberculosis of bone. Now, it is quite certain that in Norway, as in other parts of the world, two-thirds of the population do not bear evident traces of tuberculosis, nor do we find 55 per cent. of our population affected with swollen tuberculous glands and scars, nor even 19 per cent. with cicatrices on the cornea after tuberculous keratitis.

The objection that I have confounded lupus vulgaris with lupus erythematosus will not, I am sure, be made at this meeting. though such an argument has sometimes been put forward. The only objection which can be made against these statistics is that the number observed is not large enough. Nowadays, when the frequency of latent tuberculosis is well known the fact that one-third of the cases were not affected with positive tuberculous symptoms will not be allowed to have weight; it is in fact by no means rare for an individual who suffers from lupus erythematosus to exhibit at first no symptom of tuberculosis, but later to become positively tuberculous. I have recently recorded some cases of this kind. The fact that there is a marked history of tuberculosis in the families of patients suffering from lupus erythematosus has been specially mentioned by Mr. Jonathan Hutchinson, and the fact is often very striking, but as my own statistics on this

point are not complete I shall not dwell upon it. I think that the statistics I have given are strong evidence of an intimate connection between the discoid form of lupus erythematosus, to which hitherto I have alone referred, and tuberculosis.

The Acute Form of Lupus Erythematosus.

In the acute malignant form of the disease described by Kaposi this connection also seems very probable. Of the 11 cases originally described by Kaposi 6 ended fatally, and in 3 the cause of death was pulmonary phthisis; in the other 3 it was pleuro-pneumonia. The only case I have myself seen is one which I have recently described. The death of the patient, which occurred at an early stage, was due to pulmonary tuberculosis rapidly developed; other cases ending in the same way have been described by other authors. In Dr. Brooke's case the patient died from abdominal tuberculosis. It must, however, be admitted that in some cases, in those for instance of Petrini and Koch, tuberculosis was not demonstrated.

Certain Allied Skin Affections of Undoubted Tuberculous Origin.

There is another argument which pleads strongly for the dependence of this disease upon tuberculosis, and that is that there are certain skin affections undoubtedly tuberculous in origin which are to be found intermingled in such a manner with lupus erythematosus that an intimate relationship between them cannot be denied. These affections are allied on the one side to lupus erythematosus and on the other to lichen scrofulosorum (Hebra). There is, in fact, an uninterrupted series of transition forms linking these two diseases together. The forms bordering on discoid lupus erythematosus were described by Mr. Jonathan Hutchinson in the second of his Clinical Lectures upon lupus erythematosus.* I have myself described the same affection as a peculiar form of lupus erythematosus disseminatus, because (1) the efflorescences, the fundamental type of which is an erythematous lesion, may be found scattered over the whole body; (2) I

* The "Philip Holmes Group," pp. 298 and 370.

have found them accompanied by erysipelas perstans (Kaposi); and (3) the microscopical changes are in complete agreement with the tissue changes found in discoid lupus erythematosus. Now these forms are almost always combined more or less with the acne-like and necrotic forms, which, as Hebra in his work on skin diseases pointed out, occur very often in combination with his lichen scrofulosorum. In some cases the erythematous element prevails, in others the necrotic and pustular. Special and attentive observations on this point for the last twenty years have convinced me that discoid lupus erythematosus is linked with lichen scrofulosorum in such a way that we cannot at any point cut the chain without doing violence to Nature. These forms are in France called "folliclis," granuloma innominata, and by other names. In recent years they have been described by many British writers as acne scrofulosorum or acne-like scrofulides. During the present year Dr. Johnston and Dr. Allen in America have described forms belonging to this group, but bordering more on lupus erythematosus, as necrosing chilblains and necrotic granulomata. These forms, too, may, as I have said, be accompanied by erysipelas perstans (Kaposi), and may be found connected both with common discoid lupus erythematosus and with the acute fatal form of Kaposi. It seems to me that these facts also afford strong evidence of the connection between lupus erythematosus and tuberculosis.

The Exanthems of Tuberculosis.

I will here digress to refer to two skin affections belonging to the group to which I have applied the term "the exanthems of tuberculosis." (1) The first is the not very frequent eczematous variant of lichen scrofulosorum, to which I have proposed to apply the term "eczema scrofulosorum." (2) The other is one of the most common skin affections to be met with in children; this is the well known whitish macules and scaly spots to be seen on the face of young people and children, the so-called pityriasis simplex or alba. The transition from lichen scrofulosorum through eczema scrofulosorum to this affection is easily traced. The importance of the recognition of this fact is obvious, since the practitioner, especially

the general practitioner, will meet with this lesion every day in his practice. If he recognises it he may do much good by advising special care in the case of these young individuals, and may thus prevent tuberculosis from taking more dangerous forms in them.

On the whole, although it cannot be said that the dependence of lupus erythematosus upon tuberculosis is strictly proved, nevertheless I think that it is in a high degree probable, and further investigation will, I believe, finally settle the question.

The Toxæmic Tuberculous Theory.

If the probability of such connection be granted, it remains to find an explanation. It may be said, and the possibility cannot of course be excluded, that tuberculous infection may here play only a predisposing part, and that the disease itself may be caused by another unknown infection which is favoured by tuberculosis, but I see no reason for having recourse to this hypothesis when we have the well known tubercle bacillus present in the body, and when the existence of this infection will easily account for all the symptoms of the disease. It has been suggested, among others by Brocq, that lupus erythematosus might be produced by various different causes in people weakened and predisposed, owing to tuberculous infection, but this explanation is not satisfactory since a disease so typical as lupus erythematosus must, as it seems to me, be produced by a special and specific cause.

But while we may consider the tubercle bacillus as most probably the real and essential cause of the disease, it must be remembered that this microbe can, for reasons above given, scarcely be supposed to be, as a rule, present in the inflamed skin. There are good reasons, therefore, for looking to the circulating toxins of the bacillus. This toxin hypothesis will also account for all the clinical symptoms of the disease and all the anatomical changes found in the tissues. Clinically the first symptom observed is a very marked hyperæmia due to vasomotor disturbance evidently set up in the vasomotor centres. This can hardly be doubted when we call to mind the sudden and remarkable symmetrical eruption of erythema lupinosum (Veiel). Microscopical examination also shows

that dilatation of the vessels is the first pathological disturbance; then follows irritation of the tissue cells, both of the endothelial cells of the vessels, and of the connective tissue cells around them. These cells first show morbid proliferation, and then malnutrition. A general invasion by small migratory cells in masses may then be caused by the chemotactic effect of the abnormal products of the poisoned tissue cells; the inflammation very soon reaches a high degree. The masses of cells at first for the most part lie along the vessels, but the chorion is soon everywhere subjected to cell infiltration, and the intercellular tissue also suffers and is partially destroyed. The central atrophy and loss of substance which finally ensues may thus in part be accounted for. Besides, many blood vessels are rendered almost impermeable by the great proliferation of their endothelial cells, and finally, if the inflammation be very intense, they become the seat of true thrombosis.

Dr. Holder, of New York, has recently called attention to this thrombosis, and preparations which I have made from a deeply infiltrated patch on the cheek showed thrombosis very distinctly. The toxin theory, I think, accounts for all these lesions fairly well, and is also sufficient to account for the very chronic persistent forms. I do not therefore regard the hypothesis of M. Hallopeau as to the presence of any form of tubercle microbe in this disease to be necessary. I have never myself seen giant cells, but Dr. Audry, of Toulouse, found characteristic giant cells in two cases, and though he found no bacilli he nevertheless believes that this observation affords a new proof of the tuberculous nature of lupus erythematosus.* If true giant cells were to be found more frequently in this disease, its analogy with lichen scrofulosorum, in which they are not seldom seen, would be the more obvious. It is probable that the bacillus itself may sometimes find its way by the blood to such inflamed foci, where it is stopped. This would account for the cases in which the local reaction is produced by tuberculin injections. I have, however, never seen a transition from lupus erythematosus to lupus vulgaris. Our President, Dr. Jamieson, has put forward the suggestion that

* A case published this year by Dr. Leredde, in which giant cells were found, may be considered doubtful.

the trunks of the nerves supplying the affected regions of the skin may, as in leprosy, be invaded, and that the varied appearances met with in lupus erythematosus may be due to neuritis. But against this hypothesis are (1) the distribution of the disease, which does not affect the area supplied by special nerve trunks or branches, and (2) the absence of marked disturbances of sensation in the affected areas. I had the sensibility of the affected areas in a severe case carefully investigated, with the result that it was found that tactile sensibility and sensibility to heat were normal, sensibility to pain was found a little greater in the affected areas, as is shown by the fact that the patient better distinguished between the needle point and the needle head than on the normal skin. The hyperalgesia revealed when an attempt is made to remove scabs and crusts from the affected surface is well known. The rare condition called erysipelas perstans is probably due to some pathogenetic process different from that which produces the other skin lesions of this disease, for it is very often, I might perhaps say as a rule, non-symmetrical; further, the vasomotor paralysis is persistent and will act more deeply on the tissues. Symptoms of peripheral nerve disorder may also be found, as in a case which I have described. This condition, as well as the pleuro-pneumonia which occurs in similar cases, is always accompanied by high fever and much prostration; nevertheless, the symptoms certainly belong to the disease itself, and are not to be looked upon as accidental complications. In one instance I observed such "erysipelas" in a woman, to whom calcium sulphide was given with the hope of inducing shrinking of some large tuberculous glands. Some years earlier the same drug had produced in the same patient a very acute eruption of discoid lupus erythematosus on the face. In a girl treated in the same way for tuberculous glands, ordinary discoid lupus erythematosus appeared on the cheeks and lasted for many years. Such occurrences as these are very well accounted for by the toxin hypothesis. For when a pathogenic microbe—for instance, the bacillus of leprosy—is attacked it will respond by reacting and pouring out its toxins.

It has been argued that the toxin hypothesis is unsatisfactory because lupus erythematosus is very rare as compared to

tuberculosis, but to this I need only reply that many people take quinine, but very few suffer from quinine rash.

Nomenclature.

It seems to me that a discussion of the nomenclature of these disorders should be postponed until the etiology both of lupus erythematosus and of other skin affections related to it is more completely known.

Conclusions

1. Lupus erythematosus is always and in all its forms an eruptive inflammatory disease of which the localisations are determined by the vasomotor centres of the skin. It is never merely a local process.

2. Local irritation by heat, cold, and drugs plays only an accidental and determining part by bringing the vasomotor system into play.

3. In view of the very frequent coincidence with tuberculosis it must be admitted that the latter plays an important part in the etiology of the skin affection, and is probably the real and essential cause of it. The fact that a connection may be traced between all forms of lupus erythematosus and certain affections the dependence of which on tuberculosis is beyond doubt is an evidence for the tuberculous origin of lupus erythematosus.

4. As the tubercle bacillus cannot be proved to be present in the inflamed skin, it is probable that the inflammation is brought about through the toxins of the bacillus which act in the first place on the vasomotor centres, and in the second place on the parts of the skin in which the vasomotor disturbances are set up.

5. The main anatomico-pathological changes are vasomotor dilatation of the blood vessels, secondary poisoning of the tissue cells, and inflammation—the whole resulting very often in atrophy, rarely in necrosis.

MULTIPLE BENIGN SARKOID OF THE SKIN.

BY

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Christiania.

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The skin affection here described is, so far as I am aware, not generally recognized. I have seen two cases in Norway; one in a female many years ago of whose case I have no notes, and the example which forms the subject of this paper. A typical case in a male was presented at the Dermatological Congress in London (1896), but I do not know by whom. A majority of the experienced observers present failed to recognize the condition, so that I am not far wrong in saying that the disease is a rare one.

The only clinical description known to me which bears any resemblance to my case, is given in a recent paper by Jonathan Hutchinson in his "Archives of Surgery," October, 1898. I dare not say that the skin affection there described as "Mortimer's Malady" is identical with my case, since the latter shows some very marked clinical features not found in Mortimer's disease, and since Mr. Hutchinson has had no opportunity to examine his cases histologically. Nevertheless, I am inclined to believe that they are only variant types of the same group of diseases and perhaps, later on, they may be found to represent benign forms of so-called pseudoleucemic affections of the skin. I shall return to this discussion after having given an account of my own case.

The patient, a policeman, was presented first at the University Polyclinic in September, 1894, and the disease was almost in the same condition then as two years later, when he came to me privately. He was then 36 years old, and stated that he had always been in good health, and especially that he had never suffered from any scrofulo-tuberculous affection nor from syphilis. His children were healthy. The skin disease appeared first on the brow, spreading to other parts of the face from there. It made its appearance gradually on the scalp, trunk and limbs.

Present Condition.—The patient looked a little pale, but felt tolerably well, and his functions were normal. On the forehead and temples a number of characteristic spots and patches were visible, although they were of somewhat different appearance, varying with the stage of development they had reached. Their size ranged from that of a small pea to a large bean, and were slightly elevated above the skin surface. At first glance, therefore, one might believe that they were only slightly infiltrated, but when grasped between the fingers they were felt to penetrate deeply and to form well defined nodules and infiltrations. The surface of the smaller efflorescences was of a uniform yellowish-brown colour, sometimes slightly scaling. Somewhat larger nodules showed a slight central depression of a bluish-red tint, sharply contrasting with the border. As the growths increased in size and became large, flattened, irregularly contoured patches, the depressed centres deepened in colour and the border became narrower until it was reduced to one mm. in breadth. The large patches with their apparent atrophy could by palpitation be determined to form well defined, deep infiltrations of the skin. On close inspection a network of dilated capillaries could be seen in the central area; the interpapillary lines and lanugo hairs were also distinct. As remarked before, these patches, with their irregular contour, bluish-red centre and yellow border, presented so characteristic an appearance that they can be mistaken for no other known skin disease. Similar areas were found on the radix nasi, in front of the ears, on the cheeks, in the beard, and even in the sub-maxillary region.

On the hairy scalp there were visible everywhere a great many lesions of varying size but not so sharply outlined here as on the face. The infiltration of the skin was also less marked, at all events more difficult to demonstrate. It was only on close inspection that the patches could be made out at all. As in the beard, the growth of hair was in no way interfered with. On the neck, only three small areas could be seen on the right side below the ear, and on the left a single symmetrical spot.

The whole anterior surface of the trunk was entirely free from lesion. Between the axillary lines on the right side two small brownish spots could be detected. On the upper part

of the back, to the superior limit of the lumbar region, a great number of disseminate nodules and patches, varying in size from a pea to a bean, were to be seen, which were sometimes elevated above the skin level, sometimes not. The likeness of these lesions to the nodules of leprosy was quite close. Grasped between the fingers, the more recent were found to be infiltrated, the older not so much so. Lumbar and sacral regions were free, but on the buttocks, again, there was a number of efflorescences of the same colour as those on the back.

The eruption was confined to the extensor surfaces of the upper extremities, both forearms and upper arm. They were numerous pin-head size and larger, varying in size from a hempseed to a bean, and showed irregular outlines. It was easier to follow evolution in this situation than anywhere else. The beginning lesion, the nodules, deep-seated in the skin, already hard and dense, were rose-red in colour; they became darker later and showed some of yellowish-brown appearance at the periphery. The capillary network mentioned above appeared here also, especially in the centre of the eruptive elements. Near the shoulders, very small yellowish lesions appeared, scarcely the size of a pin-head. They were connected with the hair-follicles, were superficial and palpable with difficulty. The hands were free.

The thighs showed no signs of the disease except that on the internal surface of the left extremity and behind, just under the nates, it appeared in the form of groups of numerous, very small bluish or brownish-red flat papules. Here and there they were quite confluent, as in lichen ruber, and slightly scaling as well. These small lesions seemed to be connected with the hair-follicles. On the left thigh just above the patella a dense, hard giant nodule was visible. Over the right patella there was a flattened infiltration of irregular form and blue colour, developed partly in and around an old cicatrix of twenty years' standing. It seemed evident that it was the previous lesion which had determined the outbreak in this locality. On the legs, from knee to ankle, there were only a few large, dark brown, atrophic spots resulting from the disappearance of large nodules. On the left calf there were three such areas. On the right leg patches of an oval form

occurred on the anterior and inner side of the tibia. The feet, like the hands, were entirely free.

Lymphatic System.—The cubital lymph nodes were enormously swollen and were easily felt in size and shape, like Spanish nuts, along the inner side of the biceps from the cubitus for half the length of the arm. The axillary glands were tumified, but relatively not to so great an extent. Submaxillary glands were not swollen, and the cervical very little. The femoral nodes were so enlarged as to be visible in the fovea ovalis when the patient stood upright; the inguinal glands were not so increased in size. The spleen was never found enlarged.

The blood, I regret to say, was not so thoroughly studied as it should have been. I can only say that the number of leucocytes was a little greater than normal, especially in the case of the mononuclear cells. The number of eosinophiles was not notably increased. The urine contained no albumen or sugar.

After this description it will hardly be necessary to give *in extenso* the copious notes taken during the two or three years following, when the further development and final recovery occurred. A short summing up will be sufficient.

In October, 1896, administration of arsenic in granules (each containing 1 milligram of arsenic) was begun, and in six weeks the dose was raised to eighteen pills per diem, when a very rapid decrease of the swollen femoral glands was noticed, even by the patient himself, although no effect on the skin eruption could be detected as yet. At this time an obstinate diarrhœa, very likely occasioned by the arsenic, had set in, and so the drug had to be stopped and could be resumed only after a lapse of some weeks. Wine of iron and quinine, and in the spring cod-liver oil, were also given with the arsenic.

The last development of a new nodule in the skin occurred in the middle of December, 1896, and in January, 1897, the first evidence of beginning involution was noted. The superficial lichenoid eruption on the inside of the left thigh was rapidly fading. In April of the same year the first of the large patches began to disappear under arsenic, iron, and cod-liver oil very slowly. The large patches on the face under-

went retrogression in the period from June to October, the central area growing paler and the yellow margin fading. During this process the declivity from margin to centre became perpendicular, and the sharply drawn line so formed was often seen as a minutely denticulated zig-zag. No infiltration of the skin could be felt anywhere, but in many situations involution had left marked loss of substance. Since August, 1897, when the arsenic was stopped, the patient has taken no medicine. On April 7, 1899, I made the following note: The patient looks rather stronger than before, and feels pretty well. On the face the disease has left slightly depressed but sharply defined white cicatrices, which redden with the heat of exertion. The loss of substance on the extremities is marked and deep, the skin being thin and atrophic, following disappearance of larger lesions; in the case of the smaller it is not so noticeable. On the upper arms the trace may be somewhat hyperemic; on the back, they are yellowish; on the legs, dark brown, pigmented, and very atrophic. The cubital glands are very large, though a little reduced in size. They are quite soft. The patient has pursued his occupation during the whole course of the disease. I found him sound and healthy for the last time on July 8, 1899.

Histology—Two nodules about the size of a pea were excised for examination, one quite recent, the other in a more advanced stage. The pieces were hardened in alcohol and stained by different methods of which the eosin-methylene blue solution of Pianese gave the best picture of the process in the skin.

The first glance through the microscope was somewhat surprising. The microscopical features of the disease were as peculiar as the clinical and showed no similarity to any other skin affection which I had previously had an opportunity to examine.

Through the whole depth of the corium from the papillary layer to the limits of the subcutaneous tissue, sharply circumscribed foci of a new growth were seen separated from each other. The new formed foci were generally more widely disseminated than appears in this section, by at least relatively normal corium tissue. Closer investigation

with high power showed that the cells of the new growth were of the type of epithelioid connective-tissue cells, and that the tumour as a rule had its origin in the perivascular lymph spaces. The proliferated cells soon enclosed the greatly dilated vessels with a compact, cylindrical mass. At this early stage the cells were small and more deeply stained than the adult, but there could be no doubt as to their origin and character. As proliferation increased and the foci took different shapes, though still sharply circumscribed, the resemblance to epithelioid cells became more marked. The nuclei were large and vesicular, less deeply stained, and showed distinct nucleoli. The nuclei were sometimes multiple. The cell protoplasm was increased in amount and sent out prolongations in different directions. In a few instances I found true giant cells of the sarcomatous type. Mitosis was scarcely anywhere to be detected.

It is readily understood that this rapid proliferation in areas enclosed in dense connective tissue must derange cell nutrition. In larger foci, not only did the nuclei and protoplasm take stains less well, but cell contours became less distinct. Degeneration in the central cells was also evidenced by the appearance of granules, varying in size, staining deeply, and probably derived from the chromatin substance of the cells. The granules, without careful examination, may easily be taken for micrococci. A great many cells were destroyed and removed in this way without doubt, and in the oldest foci a marked rarification of the new growth took place, leaving a beautiful network or reticulum. Occasionally, large foci were divided by connective-tissue septa, from which reticulum was, as it were, spun out.

The growth was composed almost entirely of the epithelioid cells, but here and there a capillary vessel could be made out, its endothelium intact. A few leucocytes were seen in recent areas wandering through the tissue, but their number was always very small. "Mastcellen" were found where the process was in its earliest stage. True plasma cells did not occur.

Some foci, most frequently seen in the papillary and upper part of the reticular layer, developed, not according to the general rule from perivascular lymph spaces, but from the corium itself, independent of the vessels. These cell masses

looked less compact because a part of the collagen fibres remained, and because they stained less deeply with basic anilin dyes than those originating about vessels. A marked tendency to connective-tissue cell proliferation existed throughout the corium. Dilatation of the capillary loops of the papillæ accounts for one of the clinical appearances, the bluish colour and network of the centre of older patches.

The elastic fibres, stained with orcein, were completely destroyed everywhere in the new growth. In the surrounding tissue they appeared intact, abruptly disappearing at the point of entrance into the diseased areas.

The outer epidermis, as a whole, was not much affected by the process in the corium as might be expected, since the foci generally lay deep in the cutis. The rete over the younger nodules was attacked to the extent of levelling its interpapillary prolongations as well as the papillæ by the pressure from below. Like the outer epidermic strata, the skin appendages are little affected, the foci not often appearing in their neighbourhood.

My search for micro-organisms has produced no result. Granules were sometimes met with in the cells of such size and configuration as possibly to be mistaken for micrococci. They were now and then arranged in regular series, and occasionally took on a bacillus-like shape. They were so rare as to be of practically no consequence. No bacteria were found in the blood. Cultures and inoculations were not made; they should be done at the first opportunity.

Etiology.—As for the etiology and pathogenesis of the disease, two theories suggest themselves—that the lesions might be provoked through defective blood-formation or one or another auto-intoxication. Although no definite information could be elicited as to whether tumefaction of the lymph nodes preceded or followed the skin outbreak, it is not probable that it was the consequence of the skin process. As evidence of this, the cervical glands, in spite of many large nodules on the head, were only slightly swollen.

Summary.—It may be useful to give a short review of the features of this rare disease and compare them with other better known conditions.

Clinically, we find in a middle-aged, pale, thin man, groups

of lymph nodes much swollen, and on examination a slight augmentation of the number of white corpuscles. At the same time there exists a widespread, somewhat symmetrical eruption, firm nodules of varying size, on head and extensor surfaces of trunk and extremities. They range in size from a hemp-seed to a bean, and the larger have irregular contours. They involve the whole skin, and are movable with it. Only on the scalp is the infiltration not palpable. Here only yellowish outlines are seen. The colour of the early nodules is bright red, becoming darker and finally yellowish or brown. Slight scaling occurs on older lesions. They show a tendency to peripheral spreading and central depression. On the face they have a peculiar appearance, with blue centre and yellow border, a feature present in all the cases I have seen. The nodules disappear finally leaving, as a rule, a loss of substance in the skin, which may be white on the face, yellow on the back, and darker at the periphery on the legs. Exudation, ulceration never take place. A papular eruption grouped like lichen planus was seen on the inside of the thigh. A tendency to develop at the site of old injury should be remembered. The symmetry is not such as is found in affections whose localisation is evidently determined by central nerve influence. The disease seems to be benign, and disappears under arsenic or perhaps spontaneously.

Compared with "Mortimer's Malady," I find many points of resemblance. In the latter there is essentially the same symmetrical eruption of nodules and patches, in the same localities, a slow peripheral spread with central depression, and after long duration spontaneous involution without ulceration and with loss of substance. Hutchinson's cases had good health. He does not, however, mention swelling of lymph nodes nor the peculiar appearance of the face patches. In his cases there were diffuse subcutaneous infiltrations over the bridge of the nose and the ears. The nodules were, according to description and plates, more elevated than I have seen them. Future observation must decide to what degree these differences are essential.

The histology was also unique. The areas of new growth might be described as perivascular sarcomatoid tissue built up by excessively rapid proliferation of epithelioid connective-

tissue cells in the perivascular lymph spaces, with little addition of other varieties. The tumour soon begins to degenerate, and the tissue is rarefied, showing a network of branched connective tissue cells. It should be remembered that true giant cells of sarcomatous type were found, though rarely. Compared with other new growths of the skin, this must be said histologically to possess affinity to sarcoma and also to the very rare cases of so-called pseudoleucemia cutis described by Arning* and Max Joseph.† The new growth here described, nevertheless, seems at present to be rather *sui generis*.

It should be particularly emphasized how different the histology of this process is from that of leucemia cutis with its lymphoid tissue and small lymphoid cells.‡

As a preliminary name for the clinical and histological type here described, the term, "Multiple Benign Sarkoid," perhaps, will not be found unsuitable. It will be remembered that Max Joseph recently proposed the name sarkoid—used previously by Kaposi in a wider sense—to be applied to some special forms of sarcomatosis with fatal prognosis. (See Archiv f. Dermatol., B. 46, p. 100.)

* Verhandl. des III. Congr. der Deutsch. Dermat Gesellsch., Leipzig, 1891.

† Idem, also Deutsch. Med. Wochenschr., 1891, No. 51.

‡ See recent paper of Kreibich, Archiv f. Derm. u. Syph., B. 47. H. 2. Feb., 1899.

To Illustrate Prof. Boeck's Benign Sarkoid of the Skin.